

AD_____

Award Number: DAMD17-00-1-0262

TITLE: Genetic Counseling for Breast Cancer Susceptibility in
African American Women

PRINCIPAL INVESTIGATOR: Chanita M. Hughes, Ph.D.

CONTRACTING ORGANIZATION: University of Pennsylvania
Philadelphia, Pennsylvania 19104-6205

REPORT DATE: February 2004

TYPE OF REPORT: Annual

PREPARED FOR: U.S. Army Medical Research and Materiel Command
Fort Detrick, Maryland 21702-5012

DISTRIBUTION STATEMENT: Approved for Public Release;
Distribution Unlimited

The views, opinions and/or findings contained in this report are those of the author(s) and should not be construed as an official Department of the Army position, policy or decision unless so designated by other documentation.

20040903 061

REPORT DOCUMENTATION PAGEForm Approved
OMB No. 074-0188

Public reporting burden for this collection of information is estimated to average 1 hour per response, including the time for reviewing instructions, searching existing data sources, gathering and maintaining the data needed, and completing and reviewing this collection of information. Send comments regarding this burden estimate or any other aspect of this collection of information, including suggestions for reducing this burden to Washington Headquarters Services, Directorate for Information Operations and Reports, 1215 Jefferson Davis Highway, Suite 1204, Arlington, VA 22202-4302, and to the Office of Management and Budget, Paperwork Reduction Project (0704-0188), Washington, DC 20503

1. AGENCY USE ONLY
(Leave blank)**2. REPORT DATE**
February 2004**3. REPORT TYPE AND DATES COVERED**
Annual (22 Jan 2003 - 21 Jan 2004)**4. TITLE AND SUBTITLE**Genetic Counseling for Breast Cancer Susceptibility in
African American Women**5. FUNDING NUMBERS**

DAMD17-00-1-0262

6. AUTHOR(S)

Chanita M. Hughes, Ph.D.

7. PERFORMING ORGANIZATION NAME(S) AND ADDRESS(ES)University of Pennsylvania
Philadelphia, Pennsylvania 19104-6205**8. PERFORMING ORGANIZATION
REPORT NUMBER****E-Mail:** chanita@mail.med.upenn.edu**9. SPONSORING / MONITORING
AGENCY NAME(S) AND ADDRESS(ES)**U.S. Army Medical Research and Materiel Command
Fort Detrick, Maryland 21702-5012**10. SPONSORING / MONITORING
AGENCY REPORT NUMBER****11. SUPPLEMENTARY NOTES****12a. DISTRIBUTION / AVAILABILITY STATEMENT**

Approved for Public Release; Distribution Unlimited

12b. DISTRIBUTION CODE**13. ABSTRACT (Maximum 200 Words)**

Increasingly, the cultural beliefs and values of participants are being recognized as important factors in genetic counseling. Despite recommendations to increase the cultural sensitivity of genetic counseling, such programs have not been developed or evaluated. The objectives of this study are to develop a Culturally Tailored Genetic (CTGC) protocol for African American women and evaluate its impact on decision-making and satisfaction about BRCA1/2 testing, quality of life, and cancer control practices. A secondary objective of this study is to identify African American women who are most and least likely to benefit from CTGC vs. SGC. The key research accomplishments achieved during the past year include finalizing the culturally tailored genetic counseling protocol and initialing subject recruitment.

14. SUBJECT TERMSBehavioral/psychosocial research, BRCA1/2, decision-making, quality
of life**15. NUMBER OF PAGES**

74

16. PRICE CODE**17. SECURITY CLASSIFICATION
OF REPORT**

Unclassified

**18. SECURITY CLASSIFICATION
OF THIS PAGE**

Unclassified

**19. SECURITY CLASSIFICATION
OF ABSTRACT**

Unclassified

20. LIMITATION OF ABSTRACT

Unlimited

Table of Contents

Cover.....	1
SF 298	2
Table of Contents.....	3
Introduction.....	4
Body	4
Key Research Accomplishments	8
Reportable Outcomes.....	8
Conclusions.....	9
References.....	10
Appendices.....	10

A. INTRODUCTION

Five to 10% of all breast cancer cases have been attributed to two breast-ovarian cancer susceptibility genes called BRCA1 and BRCA2 (BRCA1/2). Genetic counseling and testing for BRCA1/2 mutations is now available through clinical research programs using standard counseling protocols. The goal of pre-test counseling is to facilitate informed decision making about whether to be tested and to prepare participants for possible outcomes. The goal of post-test counseling is to provide information about risk status, recommendations for surveillance, and options for prevention. However, previous research suggests that African American and Caucasian women differ in their attitudes about and responses to pre-test education and counseling. Increasingly, the cultural beliefs and values of participants are being recognized as important factors in genetic counseling. Despite recommendations to increase the cultural sensitivity of breast cancer risk counseling, such programs have not been developed or evaluated. Therefore, the purpose of this study is to develop a Culturally Tailored Genetic Counseling (CTGC) protocol for African American women and evaluate its impact on psychological functioning and health behaviors compared with Standard Genetic Counseling (SGC) in a randomized clinical trial. This research is linked with Dr. Hughes' Career Development Award and has the following primary technical objectives:

(1) To evaluate the relative impact of CTGC vs. SGC on decision-making and satisfaction about BRCA1/2 testing. Compared to SGC, CTGC will lead to higher rates of test acceptance and satisfaction with testing decisions. These effects will be mediated by increases in perceived benefits and decreases in perceived limitations and risks of genetic testing.

(2) To evaluate the impact of CTGC vs. SGC on quality of life and health behaviors following BRCA1/2 testing. Compared to SGC, CTGC will lead to larger decreases in general and cancer-specific distress, greater increases in adherence to cancer screening guidelines, and lower rates of prophylactic surgery. Reductions in psychological distress will be mediated by increased use of spiritual coping strategies.

Secondary Aim

To identify African American women who are most and least likely to benefit from CTGC vs. SGC. We predict that the relative benefits of CTGC will be greatest for women with greater endorsement of African American cultural values and those identified as BRCA1/2 carriers.

B. BODY

The research was transferred to the University of Pennsylvania Medical Center in February 2002 and approval for the use of human subjects was provided in February 2003. The second year of the study focused on (1) finalizing the culturally tailored genetic counseling protocol and (2) initiating subject recruitment. These activities are listed below and described in detail in the sections below. Specifically, activities related to finalizing the protocol and initiating subject recruitment are described in sections 1 and 2. Manuscripts that have been generated with grant support are described in section 3. This project is linked with Dr. Hughes' Career Development Award (CDA) and activities regarding professional development are provided in section 4.

Summary of Accomplishments During the Past Year

- Completed focus groups and pilot tests to finalize the Culturally Tailored Genetic Counseling protocol
- Initiated subject recruitment
- Evaluated accrual and response rates
- Generated manuscripts

(1) Finalizing the Culturally Tailored Genetic Counseling Protocol (CTGC). After obtaining approval for use of human subjects by the Contracting Officer in February 2003, we completed two focus groups (n=7) and pilot tested the CTGC. Our decision to complete two focus groups instead of the four planned sessions was made because we had completed quantitative work during the first year of the study to evaluate the prevalence of cultural beliefs and values among African American women. We also conducted a literature review on this topic during the previous year. The focus groups were conducted to confirm the importance of the beliefs and values that had been identified through our literature review (see section 3 below on Manuscripts) and quantitative work. Consistent with this work, issues related to the importance of family relationships emerged as a key theme during the focus groups. Specifically, participants indicated that family members were an important resource used to make decisions about health care and that past experiences, particularly those of family members affected with cancer, were also used to health care decisions. Religious and spiritual beliefs (e.g., prayer) also emerged as a central theme; participants indicated that these resources were used to make health care decisions and to cope with medical issues. Participants also expressed a need for mental health and social support services that are designed to address the needs of African American women. Although the CTGC protocol is not designed to provide clinical intervention, the themes that emerged during the focus groups provided further support for the inclusion of genograms to assess familial and spiritual issues as part of the CTGC protocol.

Pilot Testing. After conducting focus groups, the CTGC protocol was pilot tested. The purpose of the pilot test was to evaluate the effectiveness of the probes designed to address cultural beliefs and values. A secondary objective of the pilot test was to evaluate how comfortable participants would be discussing cultural beliefs and values. The protocol was pilot tested with four high-risk African American women during March-April 2004. Participants received the CTGC protocol that includes information on hereditary breast cancer and genetic testing, information about the benefits, limitations, and risks of genetic testing, and probes that are tailored to address African American cultural values related to communalism, spiritual and religious beliefs, and flexible temporal orientation. The entire protocol was delivered to each participant by the Genetic Counselor for the study; after completing the protocol, participants provided written feedback on the content of the CTGC protocol. All participants reported that it was important that health care providers take into account their beliefs and values when discussing medical options and more importantly, all participants were comfortable discussing their beliefs and values during the session. Overall, participants were extremely satisfied with the content of the CTGC protocol. After completing the pilot test and having the CTGC protocol reviewed by study consultants, the protocol was finalized.

(2) Recruitment. After the protocol was finalized, we initiated subject recruitment. Eligible subjects are African American women ages 18 and older who have a 5%-10% prior probability of having a BRCA1/2 mutation. Eligible subjects are identified by self-referral through mammography and oncology clinics located at the University of Pennsylvania and through the community-based referral network that was developed specifically for the study. Following self-referral, participants are contacted by telephone to determine eligibility using a structured baseline telephone interview. This interview takes approximately forty minutes to complete and includes measures of sociodemographic characteristics, personal and family history of cancer, perceived risk of having a BRCA1/2 gene alteration, and psychological functioning. Following completion of the baseline telephone interview, eligible subjects are invited to participate in pre-test education and counseling. Those who agree to participate in this session are randomized to receive Standard Genetic Counseling (SGC) or Culturally Tailored Genetic Counseling (CTCG). Written informed consent is obtained for participation in pre-test education and counseling. After completion of the pre-test education session, subjects who are interested in genetic testing are given an opportunity to consider their decision further and have an opportunity to meet individually with a medical oncologist as part of the standard and culturally tailored genetic counseling protocols. After the meeting with the medical oncologist, blood is drawn for genetic testing after obtaining written informed consent. Once BRCA1/2 test results are available, test results are disclosed using the protocol that is consistent with the format used to provide pre-test education and counseling (SGC or CTCG).

Accrual and Response Rates. During the past year, a total of 100 eligible subjects were identified and of these, 57 (57%) completed the baseline telephone interview and agreed to participate in the study, 12 (12%) declined to participate in the study, 13 (13%) could not be reached, and 18 (18%) are pending contact. Of the eligible women who agreed to participate in the study, 31 (54%) agreed to participate in pre-test education and counseling and 26 (46%) declined to participate in pre-test education and counseling. Of those who agreed to participate in pre-test education and counseling, 15 (48%) have been randomized to SGC and 16 (52%) have been randomized to CTGC. Nine pre-test education and counseling sessions have been completed and 22 are pending completion. In terms of sociodemographic characteristics for subjects enrolled in the study, most are under age 50 (54%) (Mean age = 49.12), not married (70%), have some college education or are college graduates (54%), and are employed (61%).

(3) Manuscripts.

Minority Recruitment in Hereditary Breast Cancer Research (Hughes C et al., Cancer Epidemiology, Biomarkers and Prevention, In press). As we began to initiate subject recruitment for the study, we reviewed the types of strategies that have been the most effective for recruiting ethnic and racial minority groups to participate in hereditary breast cancer research. This report reviews the resources that have been used to identify and recruit ethnic racial minorities to participate in hereditary breast cancer research. Specifically, we conducted a search of the PubMed database to identify published reports from epidemiological studies, clinical trials, and observational studies related to breast cancer susceptibility genes and genetic testing that recruited human subjects and reported data on the race and ethnicity of subjects. Empirical work published between 1995 and 2003 was eligible for inclusion in this review; a total of 15 articles met the inclusion criteria. Overall, hospital resources, either alone or in

combination with other resources, were used most often to identify potential subjects. Resources such as tumor registries, billing records, and clinic databases were used to identify potential subjects in 53.3% of studies. Active recruitment strategies that included methods in which investigators target subjects from a known resource (e.g., tumor registry, clinic database) were used in most of the studies that used hospital resources to identify subjects. Response rates for studies that used hospital-based resources to identify potential subjects ranged from 54% to 71%. This review suggests that there appears to be a finite number of resources and strategies to identify and recruit potential subjects to participate in hereditary breast cancer research; however, options for improving awareness about cancer genetics research among ethnic and racial minorities have not been extensively evaluated. Moreover, even though hospital-based resources may have a number of practical advantages for identifying potential subjects to participate in hereditary breast cancer research, a possible limitation of this resource is that only individuals who are patients at these medical facilities have the potential to be made aware about the availability of research studies. Thus, developing partnerships with community-based hospitals and clinic facilities may be one way to increase awareness of and access to cancer genetic research among ethnic and racial minorities.

Genetic Testing for Inherited Breast Cancer Risk in African Americans (Halbert, CH, Kessler LJ, Mitchell E, Cancer Investigation, Under Review.) As knowledge about hereditary breast cancer in African Americans increases, it will be important to understand barriers and motivations for participation in genetic counseling and testing. Therefore, we conducted a literature review to synthesize research on the psychological aspects of genetic counseling and BRCA1/2 testing in African Americans. Empirical research on genetic counseling and testing for inherited breast cancer risk in African Americans that was published between 1995 and 2003 was included in this review. Overall, several studies have evaluated ethnic differences in knowledge and attitudes about genetic testing or have compared African American and Caucasian women in terms of genetic testing intentions. These studies have shown that knowledge about breast cancer genetics and exposure to information about the availability of testing is low among African American women, while expectations about the benefits of genetic testing are endorsed highly. However, much less is known about the influence of cultural beliefs and values on decision-making about genetic testing or psychological and behavioral outcomes of BRCA1/2 risk information among this population. Additional research is needed to understand barriers and motivations for participating in genetic testing in African Americans. The lack of studies on psychological functioning and cancer prevention and control behaviors following testing is a significant void; however, for these studies to be conducted, greater access to genetic counseling and testing in African Americans is needed.

(4) Career Development Activities. Because this project is linked with Dr. Hughes' career development award, a summary of the professional development activities that were completed during the past year is included in this report. During the past year, Dr. Hughes has continued to be an integral member of the Abramson Cancer Center at the University of Pennsylvania. Her research on culturally tailored protocols for genetic counseling in African American women has allowed Dr. Hughes to take a leadership role in developing community-based research for cancer prevention and control. She has also co-authored several peer-reviewed manuscripts related to the psychological and behavioral impact of genetic testing for inherited cancer risk. In one of these published reports, Dr. Hughes evaluated the impact of genetic test results on colon cancer

screening practices. Health behaviors following genetic counseling are primary outcomes of this study; the experiences learned through working on these publications will facilitate Dr. Hughes' ability to generate peer-reviewed publications based on the data from this project. Dr. Hughes has also been invited to deliver presentations at one international scientific conference and at several other local scientific conferences during the past year.

C. KEY RESEARCH ACCOMPLISHMENTS

During the past year, our efforts have focused on finalizing the CTGC and initiating subject recruitment. While we completed preliminary work on the prevalence of cultural beliefs and values during 2003 and developed the content for the CTGC protocol, we believed that it was important to confirm that cultural beliefs and values related to family relationships, temporal orientation, and religion and spirituality would resonant with African American women before finalizing the protocol. Therefore, we completed focus groups and pilot tested the intervention during the past year to finalize the CTGC protocol. These activities provided further support for incorporating discussion of cultural beliefs and values related to family relationships, temporal orientation, and spirituality and religion into the CTGC protocol. We have also initiated subject recruitment and during the past year, we have identified a total of 100 eligible subjects and have randomized eligible subjects who completed the baseline to receive either SGC or CTCG. While 54% of eligible women have enrolled in the study thus far, this participation rate is consistent with enrollment rates reported in other studies on decision-making about genetic testing for inherited breast cancer risk (Lerman et al., 1996). Moreover, in other studies a comparable number of eligible women were identified during a 4-year period (Thompson et al., 2002); however, we have identified a sizeable number of eligible women during a 1-year period. Thus, we believe that our community-based referral network is an effective resource for identifying eligible subjects. To enhance our recruitment efforts during the next year, we have recruited a Senior Project Director with considerable expertise in recruiting African Americans to participate in medical research and have hired additional project staff to complete subject recruitment activities. In addition, we are assembling a Community Advisory Committee consisting of African American breast cancer survivors to provide guidance on the development of strategies to enhance study enrollment. We have also expanded our community-based referral network by adding sites within the Abramson Cancer Center Network that treat a large proportion of African American women diagnosed with breast cancer. We are confident that these activities will allow us to accomplish our accrual goals. Despite the delays that have occurred as a result of transferring the grant to a new institution and receiving approval for the use of human subjects, we have finalized the CTGC protocol and initiated subject recruitment during the past year. We have also been productive in terms of scholarship; we have published a total of four peer-reviewed papers with grant support, two of which were published during the past year.

D. REPORTABLE OUTCOMES

Manuscripts Published with Grant Support During the Past Year

Hughes C, Peterson SK, Ramirez AG, Gallion KJ, McDonald P, Skinner S, Bowen D. Minority recruitment in hereditary breast cancer research. *Cancer Epidemiology, Biomarkers and Prevention*. In press.

Halbert CH, Wenzel L, Lerman C, Peshkin BN, Narod S, Marcus A, Corio C, Demarco T, Bellamy S. Predictors of participation in psychosocial telephone counseling following genetic testing for BRCA1 and BRCA2 mutations. *Cancer Epidemiology, Biomarkers, and Prevention*. In press.

Manuscripts Published as Part of Career Development Activities During the Past Year

Halbert CH, Schwartz MD, Wenzel L, Narod S, Peshkin BN, Cella D, Lerman C. Predictors of cognitive appraisals following genetic testing for BRCA1 and BRCA2 mutations. *Journal of Behavioral Medicine*. In press.

Halbert CH, Lynch H, Lynch J, Main D, Kucharski S, Rustgi AK, Lerman C. Colon cancer screening practices following genetic testing for hereditary nonpolyposis colon cancer (HNPCC) mutations. *Archives of Internal Medicine*. In press.

Schwartz MD, Kaufman E, Peshkin B, Isaacs C, Hughes C, Finch C, DeMarco T, Lerman C. Ovarian cancer screening and prophylactic surgery in a clinic-based sample of women following BRCA1/2 testing. *Journal of Clinical Oncology*. 2003;21:4034-4041.

Manuscripts Under Review and in Preparation

Halbert CH, Kessler LJ, Mitchell E. Genetic testing for inherited breast cancer risk in African Americans. *Cancer Investigation*. Under Review.

Halbert CH, Kessler LK, Collier A, Weathers B, Smith C. African American participation in hereditary breast cancer research. Manuscript in preparation.

Halbert CH, Kessler LK, Collier A. Influence of cultural beliefs on attitudes about genetic testing. Manuscript in preparation.

Kessler LK, Fasaye G, Collier A, Halbert CH. Development of a culturally tailored genetic counseling protocol for African American women. Manuscript in preparation.

Invited Lectures and Presentations Delivered by Dr. Hughes

"Genetic Testing for Cancer Risk: Decisions and Outcomes." Oncology Institute, Bari, Italy, 2003

"Psychosocial Telephone Counseling: An Opportunity for Tailored Communications." American Society of Human Genetics 53rd Annual Meeting, Los Angeles, CA, 2003.

"Genetic Counseling for Inherited Breast Cancer Susceptibility." Psychiatry Grand Rounds, Memorial Sloan-Kettering Cancer Center, New York, NY, 2004.

E. CONCLUSIONS AND FUTURE PLANS

During the past year, our activities have focused on finalizing the CTGC protocol and initiating subject recruitment. The past year of the study has been productive and we have achieved a

number of significant accomplishments. First, we have demonstrated that it is possible to identify African American women eligible for participation in hereditary breast cancer research through a community-based referral network. African Americans have been under-represented in hereditary breast cancer research and in the majority of this research; potential subjects are identified through hospital-based resources using active recruitment strategies in which subjects are identified from clinic lists and tumor registries. We have been able to identify 100 African American women who are eligible for participation in this study through a community-based referral network in which potential subjects self-refer for study enrollment. Identification of eligible subjects is the first, and most critical step, of achieving the accrual goals for empirical research. This is a significant challenge that has been described in prior reports. During the past year, we have minimized this barrier and have identified a sizeable number of eligible subjects by self-referral through a community-based network. We have also developed a genetic counseling protocol that is tailored to the cultural beliefs and values of African American women. Although the role of cultural factors is increasingly being recognized as important determinants of cancer prevention and control behaviors, limited information is available on how to address these issues using a structured format. Our work during the past year to finalize the CTGC protocol provides methodology for how to develop culturally tailored protocols. During the next year of the project, we will continue to accrue subjects and perform data analysis to address our study aims. These results will be presented at scientific conferences and prepared for publication.

F. REFERENCES

Lerman C, Narod S, Schulman K, Hughes C, et al. BRCA1 testing in families with hereditary breast-ovarian cancer: A prospective study of patient decision-making and outcomes. *JAMA*. 1996; 275:1885-1892.

Thompson HS, Valdimarsdottir HB, Duteau-Buck C, et al. Psychosocial predictors of BRCA counseling and testing decisions among urban African American women. *Cancer Epidemiology, Biomarkers Prevention* 2002; 11:1579-1585.

G. APPENDICES

See attached for manuscripts published with grant support.

Minority Recruitment in Hereditary Breast Cancer Research

Chanita Hughes¹, Susan K. Peterson², Amelie Ramirez³, Kipling J. Gallion³,

Paige Green McDonald⁴, Celette Sugg Skinner⁵, Deborah Bowen⁶

¹Abramson Cancer Center and Department of Psychiatry, University of Pennsylvania, Philadelphia, PA

²Department of Behavioral Science, University of Texas M. D. Anderson Cancer Center, Houston, TX

³Chronic Disease Prevention and Control Research Center, Baylor College of Medicine, Houston, TX

⁴Division of Cancer Control and Population Sciences, National Cancer Institute, Bethesda, MD

⁵Department of Surgery, Duke University Medical Center, Durham, NC

⁶Fred Hutchinson Cancer Research Center, Seattle, WA

CORRESPONDING AUTHOR: Chanita Hughes, Ph.D., University of Pennsylvania, 3535

Market Street, Suite 4100, Philadelphia, PA 19104

Telephone – (215) 746-7144 / Fax – (215) 746-7140 / Email – chanita@mail.med.upenn.edu

ABSTRACT

Although recruitment of ethnic and racial minorities in medical research has been evaluated in several studies, much less is known about the methods used to recruit these populations to participate in cancer genetics research. This report reviews the resources that have been used to identify and recruit ethnic racial minorities to participate in hereditary breast cancer research. Overall, hospital-based resources were used most often to identify potential subjects and active recruitment methods were used most often to enroll eligible subjects. This review suggests that there appears to be a finite number of resources and strategies to identify and recruit potential subjects to participate in cancer genetics research; however, options for improving awareness about cancer genetics research among ethnic and racial minorities have not been extensively evaluated. To study ethnic and racial minority participation in cancer genetics research, stronger evaluation components will need to be integrated into research methods. Both observational and experimental studies are needed to determine resources that are most effective for identifying potential subjects who are ethnic and racial minorities and to evaluate the effects of different recruitment strategies on enrollment decisions among these populations.

INTRODUCTION

Each year thousands of individuals are diagnosed with breast cancer [1] and the discovery of BRCA1 and BRCA2 (BRCA1/2) susceptibility genes has catalyzed research on the clinical, ethical, and psychological implications of genetic testing for inherited breast cancer risk. Although only about 5-10% of all breast cancer cases are due to BRCA1/2 mutations, women who carry a risk conferring gene alteration have an estimated 55%-85% increased lifetime risk of developing breast cancer and a 15% to 60% increased lifetime risk of developing ovarian cancer [2-5]. It is now possible for individuals from all ethnic and racial backgrounds who have a personal and family history of breast cancer that is suggestive of hereditary disease to learn if they carry a predisposing mutation for breast cancer risk.

To date, a substantial amount of research has been conducted to understand rates and predictors of genetic test acceptance and to evaluate the clinical, psychological, and behavioral impact of genetic risk information [6-12]. These studies have shown that many, but not all, high-risk individuals obtain genetic testing for BRCA1/2 mutations and genetic test acceptance is higher among individuals who have greater perceived risks of developing cancer and those with higher levels of familial cohesion [7,9]. While there is limited evidence that receiving testing generates adverse psychological effects [6,10,13], recent studies have shown that BRCA1/2 test results may generate specific emotional concerns among mutation carriers [14,15]. Further, while early studies indicated that genetic testing for inherited breast cancer risk had a limited impact on cancer screening and prevention behaviors [11], more recent work has shown that genetic test results may motivate use of cancer screening among mutation carriers [12]. Despite the significance of these studies, the under-representation of ethnic and racial minorities has been a consistent limitation noted in the majority of this work. Less than 5% of participants in recent

studies on BRCA1/2 genetic test acceptance were African American [7,8], and racial and ethnic minorities were not included in early research on utilization of genetic testing for inherited breast cancer risk [6]. Similar trends have been reported in more recent research; less than 10% of participants in a national cancer genetics consortium that was designed to be representative of the US population are ethnic or racial minorities even though these groups (i.e., individuals who are of Black African, Asian and Pacific Islander, Latino or Hispanic, and Native American/American Indian descent)¹ comprise 25% of the US population [16].

The under-representation of racial and ethnic minorities in research studies has been addressed in a substantial number of studies; this work has described several social, psychological, and structural barriers to ethnic and racial minority participation in medical research. These barriers include mistrust of the medical community and the research process, lack of knowledge and awareness about research studies, poor economic status, and cultural and linguistic factors [17-22]. Although much less is known about barriers to ethnic and racial minority participation in cancer genetics research, previous studies suggest that similar barriers may reduce ethnic and minority participation in these studies. For example, Hughes and colleagues found that among African American women who had a college education, those who reported concerns about being exploited were significantly less likely to participate in an education session about hereditary breast cancer and genetic testing compared to women who reported no concerns². This study also found that African American women who were younger

¹Bowen D. Minority recruitment in the Cancer Genetics Research: identification of problems and opportunities for new research. Presentation at the Cancer Genetics Network Steering Committee Meeting, Reston, VA, 2002.

²Hughes, C., Lerman, C., Benkendorf, J. Participation of African American women in BRCA1 pre-test education. Paper presented at the American Society of Preventive Oncology Annual Conference. Bethesda, MD, 1998.

ages and those who had lower incomes and greater levels of cancer-specific distress were most likely to decline participation in cancer genetics education. Moreover, even though similar strategies were used to recruit African American and Caucasian subjects to participate in a randomized trial that compared different methods of providing education about hereditary breast cancer, African American women were significantly less likely than Caucasian women to self-refer for study participation [23].

Because of the importance of voluntariness in decisions to participate in research overall, and in studies that involve genetic testing in particular [24,25], self-referral is a common method for recruiting subjects into cancer genetics studies [7,8]. However, not all studies related to hereditary breast cancer involve genetic testing; other methods have been suggested to increase participation in research among ethnic and racial minorities. These methods include identifying subjects through physician referrals, tumor registries, community outreach, and targeted recruitment materials [20,26]. Each of these approaches has a number of advantages and disadvantages. For example, physician referrals may be effective because health care providers have access to both personal and family medical history and can readily identify individuals who are eligible for study participation [27,28]. Similarly, tumor registries and hospital records may be effective for identifying racial and ethnic minorities because they contain demographic and clinical information that can facilitate identification of potential subjects. On the other hand, disadvantages of physician referral and tumor registry approaches may include physician mistrust of the sponsoring institution and limited representation of ethnic and racial minorities in the patient populations at medical facilities. Other approaches that have been suggested include community outreach and mass media [29-32]. However, limited information is available on the

resources that are used to identify ethnic and racial minorities for participation in cancer genetics research.

Study recruitment is a complex process that involves determination of ascertainment sites, development of enrollment procedures, identification of study participants, and implementation of procedures for subject retention³. These activities can be conceptualized within a larger framework of study recruitment that includes mechanisms to enhance awareness about the research, acceptance of study procedures, and access to study sites among potential subjects [33]. According to this model, awareness includes understanding the procedures involved in the study while acceptability and access encompass community support for the research and one's ability to overcome practical barriers (e.g., transportation) to study participation, respectively [33]. While awareness has been conceptualized as understanding the procedures involved in participating in a study [33], awareness may also include knowledge about the availability of research studies. Outreach strategies and personalized recruitment approaches have been suggested as possible methods to increase awareness about cancer research in ethnic and racial minority groups [33]; however, information on the methods that have been used to recruit these populations to participate in cancer genetics research is not available.

To guide future efforts to recruit ethnic and racial minority groups for participation in cancer genetics research, we conducted a review of the literature to describe the resources that have been used to identify ethnic and racial minority groups for participation in hereditary breast cancer research and the strategies that have been used to recruit these populations. Specifically, to address the question of what types of resources and strategies are used to recruit ethnic and

³Ramirez, A. G., McDonald, P., Chapa, M, Gallion, K. Minority recruitment to clinical trials. Presented at the Cancer Genetics Network Steering Committee Meeting, Reston, VA, 2002.

minorities for hereditary breast cancer studies, we first describe the resources that have been used to identify subjects and then report on the methods that were used for study recruitment. Because investigators with NIH-funded research projects are required to report enrollment of racial and ethnic minority groups, we also summarize enrollment rates for these populations to provide information on the yield of subjects enrolled using various strategies. Developing a better understanding of the methods that have been used to recruit ethnic and racial minorities into hereditary breast cancer studies will help to identify potential barriers and guide future recruitment efforts to increase the generalizability of research on genetic risk factors for cancer.

METHODS

We conducted a search of the PubMed database for articles published 1995 to 2003, via a cascade method that used the broadest terms (e.g., hereditary breast cancer, genetic testing) first, with subsequent searches using more specific terms (e.g., BRCA1, BRCA2). Specifically, to identify studies related to inherited breast cancer susceptibility, we used the terms “hereditary breast cancer” in our first search and then used the terms “genetic testing, breast cancer” in our second search. In our last search, we used the terms “BRCA1” or “BRCA2.” All searches were conducted using EndNotes software to facilitate development of the reference library.

Once the reference library was created, we then conducted separate searches to identify studies with ethnically and racially diverse samples. We first used the terms “race” or “ethnic” to identify the initial set of studies and then repeated the search using specific racial and ethnic group categories (e.g., African American, Hispanic, Asian American). Duplicate citations were deleted.

Published reports from epidemiological studies, clinical trials, and observational studies related to breast cancer susceptibility genes and genetic testing that recruited human subjects and reported data on the race and ethnicity of subjects were eligible for inclusion in this review. Specifically, studies that evaluated the prevalence of hereditary breast cancer susceptibility genes and those that explored psychosocial and behavioral issues in genetic testing (e.g., interest in genetic testing, genetic test acceptance) were eligible for inclusion. We included studies that evaluated intentions to have genetic testing for inherited breast cancer risk because initial studies focused on interest in having genetic testing until testing became available. We excluded studies that did not involve recruitment of human subjects (e.g., review articles, comments and letters, and animal studies) and those that were related to genetic aspects of cancer, but were broader in scope (e.g., HER2). Abstracts of scientific meetings were not reviewed. Because we were interested in identifying the resources and strategies that have been used to recruit racial and ethnic minority groups represented in the US population, we excluded studies in which subjects had been recruited entirely in foreign countries. We also excluded studies that only included individuals of Ashkenazi Jewish ancestry because these individuals are not categorized as racial or ethnic minorities. In this study, we defined recruitment sources as the resources that were used to identify potential subjects and recruitment strategies were defined as the procedures that were used to enroll subjects into the study. Consistent with prior research, we categorized recruitment strategies as either active or passive [34]. Active recruitment strategies included methods in which investigators targeted subjects from a known resource (e.g., tumor registry, clinic database) and passive recruitment strategies included methods in which investigators provided information about the study and individuals volunteered for study participation by

contacting research staff [34]. Recruitment through an ongoing research or clinical protocol was categorized as a passive recruitment strategy as was physician and family referral.

RESULTS

We identified 159 studies on inherited breast cancer susceptibility that met our inclusion criteria. Of these 159 studies, 38 were excluded because they did not involve recruitment of human subjects, 83 were excluded because they were conducted in foreign countries, and 10 were excluded because they only included individuals of Ashkenazi Jewish ancestry or did not include any ethnic and racial minority groups. Of the remaining 28 articles, 5 were excluded because of overlap in the sample that had been used in a study already identified for inclusion in the review and 8 did not provide sufficient information on the race or ethnicity of subjects or recruitment procedures.

The 15 articles on hereditary breast cancer included in this review are summarized in Table 1. These studies were conducted in diverse geographic locations in the US: 33.3% were conducted in southern states, 26.7% were conducted in western states, and 13.3% were conducted in northeastern states. In addition, 26.7% of studies were conducted in multiple states or internationally. More than half of studies (66.7%) (n=10) were designed to evaluate hereditary cancer (e.g., prevalence of susceptibility genes) in a specific ethnic or racial group, assessed ethnic differences the prevalence of breast cancer susceptibility genes, or compared racial groups in terms of knowledge and attitudes about genetic testing. The studies that evaluated hereditary breast cancer in a specific racial group only included African Americans. Fifty-three percent of studies evaluated psychosocial and behavioral issues in genetic testing and 47% were epidemiological studies.

Overview of Recruitment Sources

As shown in Table 1, several types of resources were used to identify potential subjects. These resources included hospital resources such as oncology clinics and tumor registries, state cancer registries, hereditary cancer registries, and high-risk cancer clinics. Other resources such as public records (e.g., motor vehicle registrations) were also used; however, this resource was used in only one case-control study to identify potential subjects who did not have a personal history of cancer [44].

Hospital-Based Resources

Overall, hospital resources, either alone or in combination with other resources, were used most often to identify potential subjects. Resources such as tumor registries, billing records, and clinic databases were used to identify potential subjects in 53.3% of studies (n=8). Active recruitment strategies were used in most of the studies that used hospital resources to identify subjects; however, the methods that were used to recruit subjects varied. For example, in the study conducted by Armstrong et al. [36], potential subjects were randomly identified from clinic and billing records and were invited to participate in the study by mail. In this study, the sample consisted of women who returned a completed survey; of the 240 women who were identified, 71% returned a completed survey and were enrolled (see Table 2). However, in the studies conducted by Thompson [49] and Donovan [38], potential subjects were identified during a clinic visit and were invited to participate in the study in-person. Lipkus and colleagues [42] used a different method to recruit subjects from hospital resources that included an institutional tumor registry and clinic database. The purpose of this study was to identify predictors of genetic test intentions in African American women with (unaffected cases) and without a family

history of cancer (unaffected controls); thus, only African American women were identified from the tumor registry and clinic databases. All potential subjects were invited to participate in the study by telephone following identification from clinic databases, but an additional procedure was implemented to recruit unaffected cases. Specifically, breast cancer cases were contacted by telephone to obtain the names and addresses of their unaffected first-degree relatives (FDRs) and to obtain permission to contact these individuals. Once permission was obtained, family members were contacted by telephone and invited to participate in the study. Although the number of unaffected cases and unaffected controls who enrolled in the study was similar, response rates for controls were lower (70%) than for cases (86%).

Benkendorf and colleagues [37] used a method that was similar to the strategy used by Lipkus et al [42] to identify and recruit unaffected FDRs of breast cancer patients; however, this study also used a passive recruitment strategy in which FDRs were informed about the study through physicians and brochures located in hospital clinics. Specifically, following physician notification or reading informational brochures about the study, individuals were instructed to contact staff members for information about the study. To be included in this study, subjects who completed a baseline telephone interview also had to participate in an education session about hereditary breast cancer and genetic testing; African American women were significantly less likely than Caucasian women to participate in the education session. The study conducted by Shih and colleagues [48] also used passive recruitment strategies. The purpose of this study was to determine the frequency of BRCA1/2 mutations in high-risk individuals; subjects were also enrolled in a genetic counseling and testing protocol. Subjects in this study were identified from hospital clinics; recruitment strategies included physician-referral, family-referral, and self-referral.

Six out of the eight (75%) studies that used hospital resources to identify subjects were designed to evaluate differences in knowledge and attitudes about genetic testing between African American and Caucasian women [37,38,42,49] or evaluated BRCA1 mutations in African Americans [45,48]. As shown in Table 2, the proportion of African American women enrolled in these studies ranged from 18% to 100%. Consistent with the wide range in the proportions of African American women included in these studies, the number of African American participants varied widely. For example, 43 African American women were enrolled in the study conducted by Benkendorf et al. [37] whereas 108 African American women were enrolled in the study conducted by Donovan and Tucker [38]. Even though the studies conducted by Panguluri et al. [45] and Shen et al. [47] were both designed to evaluate BRCA1 mutations in African Americans and both used hospital clinics to identify potential subjects, 54 subjects were enrolled in the study conducted by Shen whereas 137 subjects were enrolled in the study conducted by Panguluri. Despite differences in the sample sizes, the number of affected breast cancer cases was similar in these studies; 45 high-risk African American women were enrolled in the Panguluri study and 54 African American breast cancer cases were enrolled in the Shen study.

The proportion of ethnic and racial minority subjects in the remaining studies that used hospital clinics to identify potential subjects, but were not targeted to a specific ethnic or racial minority group also varied widely. For example, 2% of the families enrolled in the study conducted by Shih et al. [48] to determine the prevalence of BRCA1 and BRCA2 mutations in high-risk individuals were African American (n=3) and 2% were Hispanic (n=3) whereas 25% of the subjects enrolled in the study on genetic testing intentions conducted by Armstrong et al. [36] were African American (n=69) and 4% were Hispanic (n=11).

High-Risk Cancer Clinics

High-risk cancer clinics, including hereditary cancer registries, were used to identify subjects in 20% of studies. Although passive strategies in these studies included self-referral to a high-risk cancer clinic [40], passive strategies also included identifying subjects from ongoing research or clinical protocols. For example, subjects in the case-control study conducted by Narod and colleagues to evaluate the association between oral contraceptive use and breast cancer risk in BRCA1/2 mutation carriers were identified through genetic counseling and testing programs located throughout the United States and in foreign countries. To be eligible for inclusion in this study, subjects had to have had genetic testing and found to carry a risk-conferring BRCA1/2 gene alteration. While some of the subjects that were included in the survey study conducted by Kinney and colleagues [41] to evaluate knowledge about genetic testing and genetic testing intentions had genetic testing as part of their participation in a hereditary breast cancer registry; however, testing was for research purposes only and these individuals had not received genetic test results prior to their participation in the survey study. Subjects in the study conducted by Narod completed study measures as part of their appointment for genetic counseling or testing or after their clinic appointment whereas subjects in the study conducted by Kinney were invited to enroll in the study by mail and completed the survey by telephone or in-person. Subjects were enrolled into the study conducted by Gao after provision of counseling about the benefits, limitations, and risks of genetic testing.

Two of the three studies that used high-risk cancer clinics to identify subjects were targeted to a specific ethnic group [40,41]. Although both of these studies were composed only of African Americans, the study conducted by Gao included 28 subjects and the study conducted by Kinney included 95 subjects. A smaller number of ethnic and racial minorities (n=14 African

American cases and 28 African American controls) were included in the study conducted by Narod.

Other Resources

Community outreach was used in only two studies (13.3%) to identify subjects; passive strategies were used to recruit subjects in both of these studies. For example, in the study conducted by Durfy et al. [39] to evaluate knowledge about genetic testing and genetic testing intentions, subjects self-referred for study participation after hearing about the project through mass media such as radio announcements and newspaper advertisements. Because a specific objective of this study was to evaluate knowledge and attitudes about genetic testing in a demographically diverse sample, media advertisements were targeted to ethnic specific outlets such as African American newspapers and community events. Press and colleagues [46] used a similar approach to recruit subjects; individuals self-referred to the study after learning about the research through advertisements placed in newspapers and flyers displayed at community centers. Recruitment efforts were also targeted to ethnic specific events in this study.

Although similar recruitment strategies were used in the studies conducted by Press et al. [46] and Durfy et al [39], the representation of ethnic and racial minorities differed. Twenty-two percent of the sample recruited for the study conducted by Press was African American (n=54) and 25.2% were Native American (n=62) whereas 7.2% of the sample recruited for the study conducted by Durfy was African American (n=39), 1.5% was Hispanic (n=8), 1.1% was Asian or Pacific Islander (n=6) and 1.8% was Other (n=10).

State or county cancer registries were used to identify subjects in two studies (13.3%) [35,44]; however, these studies differed in the strategies that were used to recruit subjects. For example, in the study conducted Anton-Culver and colleagues, women affected with breast and

ovarian cancer were identified from a county-based cancer registry; following physician notification of intent to contact patients, an introductory letter was mailed to potential subjects. After mailing the introductory letter, potential subjects were contacted by telephone for the study invitation and to complete study measures. However, home visits were completed by nurses to collect study information following identification of potential subjects from a state cancer registry in the study conducted by Newman and colleagues [44].

As shown in Table 2, similar response rates were reported in the studies that used state or county registries to identify subject [35,44]; however, the representation of ethnic and racial minorities differed. For example, 6.9% of the sample in the study conducted by Anton-Culver was Hispanic (n=54), 5% Asian (n=40), and 0.5% African American (n=4). Hispanics were not enrolled in the study conducted by Newman; however, 42% of cases were African American (n=89) and 1% were Native American (n=2). Among controls, 42% were African American (n=79), 1% were Asian (n=2) and other (n=2).

DISCUSSION

This review described the sources and strategies that have been used to identify and recruit ethnic and racial minorities to participate in hereditary breast cancer research. Overall, hospital-based resources were used most frequently to identify potential subjects. A number of different factors are likely to be considered when making decisions about recruitment strategies (e.g., cost, staff time, and recruitment success). Because effective and efficient methods for subject recruitment are critical to achieving study goals, investigators are likely to select resources from which potential subjects can be identified quickly at minimal cost. Hospital resources contain demographic and clinical information that can facilitate identification of

potential subjects without expenditure of significant resources. This may explain why this resource was used to identify potential subjects in most of the studies in this review. The goals of the studies may have also influenced the resources that were used to identify potential subjects. More than half of the studies in this review were designed to evaluate the prevalence of BRCA1/2 genes among women with a personal history of cancer or assessed knowledge and attitudes about genetic testing among women with a family history of breast cancer. Identifying women affected with cancer at centers where they have been diagnosed and treated is likely to be the most efficient approach for identifying potential subjects with a specific risk profile or personal history of cancer.

While hospital-based resources have a number of practical advantages for identifying subjects to participate in cancer genetics research, an obvious limitation of this resource is that only individuals who are patients at the medical facility will be maintained in clinic databases and tumor registries and have the potential to be made aware about the availability of research studies. Data from national surveys have shown that ethnic and racial minorities are less likely than Caucasians to have private health insurance, have a usual source of care, and are more likely to use emergency departments as their usual source of medical care [50-52]. Thus, these groups may be under-represented in the clinic databases and tumor registries at academic medical facilities where research on genetic risk factors for cancer is likely to be conducted. Previous research has shown that compared to a cancer center tumor registry, more ethnically diverse women affected with cancer were identified to participate in survivorship studies from a tumor registry at a community-based hospital [53]. This suggests that developing partnerships with community-based hospitals may be one way to increase awareness of and access to cancer genetic research among ethnic and racial minorities. Four studies in this review that used

hospital clinics were conducted at minority medical institutions (n=2) [45,48] or in partnership with a community medical facility (n=2) [37,49]; the number of African American women enrolled in these studies ranged from 43 to 137 and response rates ranged from 54% to 71%. Thus, even when cancer genetics research is conducted at community hospitals that may have a greater number of ethnic and racial minority patients, the number of individuals who enroll in studies may still vary. Regardless of the setting in which cancer genetics research is conducted, it is important for investigators to use recruitment strategies that are effective among ethnic and racial minority groups.

In terms of recruitment approaches, active methods such as in-person recruitment from clinic populations and recruitment by mail or telephone were used most frequently; the representation of ethnic and racial minority subjects was lower in studies that used impersonal recruitment methods. For example, 49% of the sample in the Donovan and Tucker study [38], which used in-person clinic recruitment, was African American whereas 18% of the sample in the Benkendorf study [37], which used a combination of active and passive recruitment strategies, was African American. This suggests that personalized recruitment approaches might be more efficacious for recruiting ethnic and racial minority groups to participate in cancer genetics research. Previous research has shown that compared to Caucasian women diagnosed with breast cancer, African American women diagnosed with breast cancer who were identified from a hospital tumor registry were less likely to enroll in a quality of life study when recruited to participate in the study by mail [30]. Thus, active, personalized recruitment methods are possibly effective strategies for recruiting ethnic and racial minorities to participate in cancer genetics research.

Advantages of active strategies include enrollment of a more generalizable study sample and less chance for self-selection bias [34]. Active strategies that use personal approaches may also enhance awareness about cancer genetics research among ethnic and racial minorities by increasing understanding about the importance of the research and by providing potential subjects with an opportunity to ask questions about the procedures involved in study participation [33]. Personalized approaches may also minimize mistrust of the research process, which has been shown to be a barrier to ethnic and racial minority participation in research in other settings [19,20,26]. However, the effectiveness of active, personalized recruitment methods is likely to depend on whether the recruiter and potential subject are from the same ethnic or racial background. Moorman and colleagues [18] found that among women who were eligible to participate in a case-control epidemiological study of breast cancer, African American women were less likely to complete the interview when they were invited to complete the survey by a non-African American interviewer. In this review, the studies that used personalized recruitment methods did not indicate whether potential subjects and recruiters were concordant in terms of race or ethnic background. Thus, additional research is needed to determine whether the race or ethnicity of the interviewer has an effect on decisions to participate in cancer genetics research among ethnic and racial minority groups.

Although the racial or ethnic concordance between potential subjects and study recruiters may influence the effectiveness of active, personalized recruitment approaches, the yield of recruitment sources and methods may also vary depending on the study population, eligibility requirements, and study procedures. We observed that the number of racial and ethnic minorities decreased as the complexity of study participation increased. For example, although the studies conducted by Lipkus et al [42] and Thompson et al. [49], both used active recruitment strategies

and had similar eligibility requirements, enrollment rates were lower in the Thompson study (54%) relative to the Lipkus study (86%). It is possible that differences in enrollment rates for these studies may have been due to the procedures involved in participation. In the Lipkus study, subjects had to complete a telephone interview and agree to participate in an education program about breast cancer risk factors and mammography whereas subjects in the Thompson study had to complete psychological measures and consider participating in genetic counseling and testing. A recent study found that African Americans were most willing to participate in studies that did not involve invasive procedures [54]. Thus, knowledge of the role of the complexity of the study design and burden would be critical in attempts to enhance ethnic and racial minority participation in cancer genetics research. Less knowledge about hereditary breast cancer and exposure to information about genetic testing for inherited cancer risk [55] may contribute to greater concerns about genetic testing procedures among African Americans. Therefore, when implementing personalized approaches, it may also be important to consider the target population's level of exposure to new medical procedures and to identify potential barriers (e.g., cost of medical procedures, access to study sites) so that strategies are designed to address these issues.

Prior studies have shown that community outreach may be effective resources for identifying ethnic and racial minority groups for participation in cancer prevention and control research [29,31]; however, only two studies included in this review used this resource to identify potential subjects. In both of these studies, subjects were recruited by self-referrals from mass media. While both of these studies were also conducted in the Pacific Northwest (Seattle, Washington), the Durfy study [39] included a smaller number of racial and ethnic minorities compared to the study conducted by Press and colleagues [46]. This may have been due to

differences in the sampling strategies used in these studies. The Press study used a specific sampling frame to identify women from diverse ethnic backgrounds while the study conducted by Durfy used a general approach. The results of these studies suggest that even in geographic areas that are not densely populated with ethnic and racial minorities, diverse study samples can be recruited if sampling plans are designed to achieve this objective. Moreover, living in a geographic area with a large proportion of ethnic and racial minorities does not guarantee that study samples will be diverse. While North Carolina is one of the top ten states with the highest number of Black residents, African American women were over sampled in the study conducted by Newman et al to ensure sufficient representation of this population [44]. Thus, regardless of the geographic location for study sites, planning and extra time and effort may be needed to recruit ethnic and racial minorities for participation in cancer genetics studies.

Although this is the first report to review recruitment of ethnic and racial minorities for participation in research on genetic risk factors for cancer, some limitations should be considered. First, we limited our review to ethnic and racial minority participation in hereditary breast cancer research. Additional research is needed to describe ethnic and racial minority participation in research on other hereditary conditions. An additional potential limitation is that we may not have identified all studies that included ethnic and racial minorities with our search strategy. However, we used a structured search method to identify studies on hereditary breast cancer with ethnic and racial minority subjects. A final limitation is that we conducted a descriptive, not a quantitative, review of recruitment resources and methods; however, the methods used to identify and recruit subjects play a critical role in whether or not individuals are made aware about the availability of research protocols [33]. This review is an important first step that describes the resources and strategies that have been used to identify and recruit ethnic

and racial minorities to participate in research on hereditary breast cancer and the yield of subjects using these methods.

It is important to emphasize that decisions not to enroll in a study are to be respected in all individuals; however, lack of awareness about available studies decreases decision-making about study participation. One issue emerging from this report is that evaluation components should be incorporated into recruitment methods used in cancer genetics research studies. It was not possible to determine which methods were most and least effective for recruiting ethnic and racial minority groups because response rates were not reported consistently. Also, for the studies that used hospital-based resources to identify potential subjects, it could be argued that the proportion of ethnic and racial minorities who were enrolled in these studies were representative of the number of ethnic and racial minority patients who receive care at these centers. However, the proportion of these populations in these resources was not reported. As increased attention is focused on inclusion of ethnic and racial minorities in NIH-funded research [56], it will also be important to establish guidelines that can be used to determine adequate representation of ethnic and racial minorities in cancer genetics research. Previous research has based adequate representation of ethnic and racial minorities in cancer treatment clinical trials on the incidence of disease in these populations [57]; however, this approach may not be reasonable to apply in cancer genetics research, where information about the prevalence of susceptibility genes among ethnic and racial minorities may be based on a limited number of studies with small samples [40,45,47]. In addition to more specific evaluations of recruitment methods and representativeness of study samples, future research should examine reasons for refusing participation in cancer genetics research as well as retention of ethnic and racial minorities in these studies. Observational studies would be useful to determine the most effective settings

(e.g., academic medical center, community hospitals) for identifying potential subjects, while experimental study designs that compare the effects of different recruitment methods and messages would provide important information on the strategies that are most and least effective for recruiting ethnic and racial minorities to participate in cancer genetics research.

ACKNOWLEDGEMENTS

This work was supported by the NIH/National Cancer Institute grant #U24CA078156 and by Department of Defense grant #DAMD17-00-1-0262 (to CH). The Cancer Genetics Network is a multi-center consortium comprising the following centers participating in the preparation of this manuscript: Fred Hutchinson Cancer Research Center, Seattle, WA (Deborah Bowen, PhD, Principal Investigator), University of Texas M.D. Anderson Cancer Center, Houston, TX (Louise Strong, MD, Principal Investigator), University of Pennsylvania, Philadelphia, PA (Barbara Weber, MD, Principal Investigator), Duke University Medical Center, Durham, NC (Joellen Schildkraut, PhD, Principal Investigator)

REFERENCES

- [1] American Cancer Society. Cancer Facts and Figures – 2003. Atlanta, GA.
- [2] Antoniou, A., Pharoah, P. D., Narod, S., Risch, H. A., Eyfjord, J. E., Hopper, J. L., Loman, N., Olsson, H., Johannsson, O., Borg, A., Pasini, B., Radice, P., Manoukian, S., Eccles, D. M., Tang, N., Olah, E., Anton-Culver, H., Warner, E., Lubinski, J., Gronwald, J., Gorski, B., Tulinius, H., Thorlacius, S., Eerola, H., Nevanlinna, H., Syrjakoski, K., Kallioniemi, O. P., Thompson, D., Evans, C., Peto, J., Lalloo, F., Evans, D. G., and Easton, D. F. Average risks of breast and ovarian cancer associated with BRCA1 or BRCA2 mutations detected in case series unselected for family history: a combined analysis of 22 studies. *Am J Hum Genet*, 72: 1117-30, 2003.
- [3] Struwing, J. P., Hartge, P., Wacholder, S., Baker, S. M., Berlin, M., McAdams, M., Timmerman, M. M., Brody, L. C., and Tucker, M. A. The risk of cancer associated with specific mutations of BRCA1 and BRCA2 among Ashkenazi Jews. *N Engl J Med*, 336: 1401-8, 1997.
- [4] Easton, D. F., Ford, D., and Bishop, D. T. Breast and ovarian cancer incidence in BRCA1-mutation carriers. *Am J Hum Genet*, 56: 265-71, 1995.
- [5] Ford, D., Easton, D. F., Stratton, M., Narod, S., Goldgar, D., Devilee, P., Bishop, D. T., Weber, B., Lenoir, G., Chang-Claude, J., Sobol, H., Teare, M. D., Struwing, J., Arason, A., Scherneck, S., Peto, J., Rebbeck, T. R., Tonin, P., Neuhausin, S., Barkardottir, R., Eyfjord, J., Lynch, H., Ponder, B. A., Gayther, S. A., Bierch, J. M., Lindblom, A., Stoppa-Lyonnet, D.,

Bignon, Y., Borg, A., Hamann, U., Hait, N., Scott, R. J., Maugard, C. M., Vasen, H., Seitz, S., Cannon-Albright, L. A., Schofield, A., Zelada-Hedman, M., and the Breast Cancer Linkage Consortium. Genetic heterogeneity and penetrance analysis of the BRCA1 and BRCA2 genes in breast cancer families. *Am J Hum Genet*, 62: 676-89, 1998.

[6] Lerman, C., Narod, S., Schulman, K., Hughes, C., Gomez-Caminero, A., Bonney, G., Gold, K., Trock, B., Main, D., Lynch, J., Fulmore, C., Snyder, C., Lemon, S. J., Conway, T., Tonin, P., Lenoir, G., and Lynch, H. BRCA1 testing in families with hereditary breast-ovarian cancer. A prospective study of patient decision making and outcomes. *JAMA*, 275: 1885-92, 1996.

[7] Schwartz, M. D., Hughes, C., Roth, J., Main, D., Peshkin, B. N., Isaacs, C., Kavanagh, C., and Lerman, C. Spiritual faith and genetic testing decisions among high-risk breast cancer probands. *Cancer Epidemiol Biomarkers Prev*, 9: 381-5, 2000.

[8] Armstrong, K., Calzone, K., Stopfer, J., Fitzgerald, G., Coyne, J., and Weber, B. Factors associated with decisions about clinical BRCA1/2 testing. *Cancer Epidemiol Biomarkers Prev*, 9: 1251-4, 2000.

[9] Biesecker, B. B., Ishibe, N., Hadley, D. W., Giambarresi, T. R., Kase, R. G., Lerman, C., and Struwing, J. P. Psychosocial factors predicting BRCA1/BRCA2 testing decisions in members of hereditary breast and ovarian cancer families. *Am J Med Genet*, 93: 257-63, 2000.

- [10] Schwartz, M. D., Peshkin, B. N., Hughes, C., Main, D., Isaacs, C., and Lerman, C. Impact of BRCA1/BRCA2 mutation testing on psychologic distress in a clinic-based sample. *J Clin Oncol*, 20: 514-20, 2002.
- [11] Lerman, C., Hughes, C., Croyle, R. T., Main, D., Durham, C., Snyder, C., Bonney, A., Lynch, J. F., Narod, S. A., and Lynch, H. T. Prophylactic surgery decisions and surveillance practices one year following BRCA1/2 testing. *Prev Med*, 31: 75-80, 2000.
- [12] Botkin, J. R., Smith, K. R., Croyle, R. T., Baty, B. J., Wylie, J. E., Dutson, D., Chan, A., Hamann, H. A., Lerman, C., McDonald, J., Venne, V., Ward, J. H., and Lyon, E. Genetic testing for a BRCA1 mutation: prophylactic surgery and screening behavior in women 2 years post testing. *Am J Med Genet*, 118: 201-9, 2003.
- [13] Croyle, R. T., Smith, K. R., Botkin, J. R., Baty, B., and Nash, J. Psychological responses to BRCA1 mutation testing: preliminary findings. *Health Psychol*, 16: 63-72, 1997.
- [14] Cella, D., Hughes, C., Peterman, A., Chang, C. H., Peshkin, B. N., Schwartz, M. D., Wenzel, L., Lemke, A., Marcus, A. C., and Lerman, C. A brief assessment of concerns associated with genetic testing for cancer: the multidimensional impact of cancer risk assessment (MICRA) questionnaire. *Health Psychol*, 21: 564-72, 2002.
- [15] Dorval, M., Patenaude, A. F., Schneider, K. A., Kieffer, S. A., DiGianni, L., Kalkbrenner, K. J., Bromberg, J. I., Basili, L. A., Calzone, K., Stopfer, J., Weber, B. L., and Garber, J. E.

Anticipated versus actual emotional reactions to disclosure of results of genetic tests for cancer susceptibility: findings from p53 and BRCA1 testing programs. *J Clin Oncol*, 18: 2135-42, 2000.

[16] US Census Bureau. United States Census 2000. US Department of Commerce. Economics and Statistics Administration.

[17] Advani, A. S., Atkeson, B., Brown, C. L., Peterson, B. L., Fish, L., Johnson, J. L., Gockerman, J. P., and Gautier, M. Barriers to the participation of African-American patients with cancer in clinical trials: a pilot study. *Cancer*, 97: 1499-506, 2003.

[18] Moorman, P. G., Newman, B., Millikan, R. C., Tse, C. K., and Sandler, D. P. Participation rates in a case-control study: the impact of age, race, and race of interviewer. *Ann Epidemiol*, 9: 188-95, 1999.

[19] Corbie-Smith, G., Thomas, S. B., Williams, M. V., Moody-Ayers, S. Attitudes and beliefs of African Americans toward participation in medical research. *J Gen Intern Med*, 14: 537-46, 1999.

[20] Gamble, V. N. Under the shadow of Tuskegee: African Americans and health care. *Am J Public Health*, 87: 1773-8, 1997.

- [21] Shavers-Hornaday, V. L., Lynch, C. F., Burmeister, L. F., and Torner, J. C. Why are African Americans under-represented in medical research studies? Impediments to participation. *Ethn Health*, 2: 31-45, 1997.
- [22] Giuliano, A. R., Mokuau, N., Hughes, C., Luna, G. T., Risendal, B., Ho, R. C. S., Prewitt, T. E., McCaskill-Stevens, W. J. Participation of minorities in cancer research: the influence of structural, cultural, and linguistic factors. *Annals of Epidemiology*, 10: S22-S34, 2000.
- [23] Lerman, C., Hughes, C., Benkendorf, J. L., Biesecker, B., Kerner, J., Willison, J., Eads, N., Hadley, D., and Lynch, J. Racial differences in testing motivation and psychological distress following pretest education for BRCA1 gene testing. *Cancer Epidemiol Biomarkers Prev*, 8: 361-7, 1999.
- [24] Geller, G., Botkin, J. R., Green, M. J., Press, N., Biesecker, B. B., Wilfond, B., Grana, G., Daly, M. B., Schneider, K., and Kahn, M. J. Genetic testing for susceptibility to adult-onset cancer. The process and content of informed consent. *JAMA*, 277: 1467-74, 1997.
- [25] Nelson, R. M., and Merz, J. F. Voluntariness of consent for research: an empirical and conceptual review. *Med Care*, 40: 69-80, 2002.
- [26] Swanson, G. M., and Ward, A. J. Recruiting minorities into clinical trials: toward a participant-friendly system. *J Natl Cancer Inst*, 87: 1747-59, 1995.

- [27] McCaskill-Stevens, W., Pinto, H., Marcus, A. C., Comis, R., Morgan, R., Plomer, K., and Schoentgen, S. Recruiting minority cancer patients into cancer clinical trials: a pilot project involving the Eastern Cooperative Oncology Group and the National Medical Association. *J Clin Oncol*, 17: 1029-39, 1999.
- [28] Bastani, R., Maxwell, A., Bradford, C. A tumor registry as a tool for recruiting a multi-ethnic sample of women at high risk for breast cancer. *J Registry Manage*, 23: 74-8, 1996.
- [29] Blumenthal, D. S., Sung, J., Coates, R., Williams, J., and Liff, J. Recruitment and retention of subjects for a longitudinal cancer prevention study in an inner-city black community. *Health Serv Res*, 30: 197-205, 1995.
- [30] Ashing-Giwa, K. The recruitment of breast cancer survivors into cancer control studies: a focus on African-American women. *J Natl Med Assoc*, 91: 255-60, 1999.
- [31] Lewis, C. E., George, V., Fouad, M., Porter, V., Bowen, D., Urban, N. Recruitment strategies in the women's health trial: feasibility study in minority populations. *Control Clin Trials*, 19: 5, 1998.
- [32] Stallings, F. L., Ford, M. E., Simpson, N. K., Fouad, M., Jernigan, J. C., Trauth, J. M., and Miller, D. S. Black participation in the Prostate, Lung, Colorectal and Ovarian (PLCO) Cancer Screening Trial. *Control Clin Trials*, 21: 379S-389S, 2000.

- [33] Brown, B. A., Long, H. L., Gould, H., Weitz, T., and Milliken, N. A conceptual model for the recruitment of diverse women into research studies. *J Womens Health Gend Based Med*, 9: 625-632, 2002.
- [34] Lee, R. E., McGinnis, K. A., Sallis, J. F., Castro, C. M., Chen, A. H., and Hickmann, S. A. Active vs. passive methods of recruiting ethnic minority women to a health promotion program. *Ann Behav Med*, 19: 378-84, 1997.
- [35] Anton-Culver, H., Cohen, P. F., Gildea, M. E., and Ziogas, A. Characteristics of *BRCA1* mutations in a population-based case series of breast and ovarian cancer. *Eur J Cancer*, 36: 1200-08, 2000.
- [36] Armstrong, K., Weber, B., Ubel, P. A., Guerra, C., and Schwartz, J. S. Interest in *BRCA1/2* Testing in a Primary Care Population. *Prev Med*, 34: 590-95, 2002.
- [37] Benkendorf, J. L., Reutenauer, J. E., Hughes, C. A., Eads, N., Willison, J., Powers, M., and Lerman, C. Patients' attitudes about autonomy and confidentiality in genetic testing for breast-ovarian cancer susceptibility. *Am J Med Genet*, 73: 296-303, 1997.
- [38] Donovan, K. A., and Tucker, D. C. Knowledge about genetic risk for breast cancer and perceptions of genetic testing in a sociodemographically diverse sample. *J Behav Med*, 23: 15-36, 2000.

- [39] Durfy, S. J., Bowen, D. J., McTiernan, A., Sprieder, J., and Burke, W. Attitudes and interest in genetic testing for breast and ovarian cancer susceptibility in diverse groups of women in western Washington. *Cancer Epidemiol Biomarkers Prev*, 8: 369-75, 1999.
- [40] Gao, Q., Tomlinson, G., Cummings, Das, S., Cummings, S., Sveen, L., Fackenthal, J., Schumm, P., and Olopade, O. I. Prevalence of BRCA1 and BRCA2 mutations among clinic-based African American families with breast cancer. *Hum Genet*, 107: 186-91, 2000.
- [41] Kinney, A. Y., Croyle, R. T., Dudley, W. N., Bailey, C. A., Pelias, M. K., and Neuhausen, S. L. Knowledge, attitudes, and interest in breast-ovarian cancer gene testing: a survey of a large African-American kindred with a BRCA1 mutation. *Prev Med*, 33: 543-51, 2001.
- [42] Lipkus, I. M., Iden, D., Terrenoire, J., and Feaganes, J. R. Relationships among breast cancer concern, risk perceptions, and interest in genetic testing for breast cancer susceptibility among African-American women with and without a family history of breast cancer. *Cancer Epidemiol Biomarkers Prev*, 8: 533-39, 1999.
- [43] Narod, S. A., Dube, M-A., Klijn, J., Lubinski, J., Lynch, H. T., Ghadirian, P., Provencher, D., Heimdal, K., Moller, P., Robson, M., Offit, K., Isaacs, C., Weber, B., Friedman, E., Gershoni-Baruch, R., Rennert, G., Pasini, B., Wagner, T., Daly, M., Garber, J. E., Neuhausen, S. L., Ainsworth, P., Olsson, H., Evans, G., Osborne, M., Couch, F., Foulkes, W. D., Warner, E.,

Kim-Sing, C., Olopade, O., Tung, N., Saal, H. M., Weitzel, J., Merajver, S., Gauthiers-Villars, M., Jernstrom, H., Sun, P., and Brunet, J-S. Oral contraceptives and the risk of breast cancer in BRCA1 and BRCA2 mutation carriers. *J Natl Cancer Inst*, 94: 1773-79, 2002.

[44] Newman, B., Mu, H., Butler, L. M., Milikan, R. C., Moorman, P. G., and King, M-C. Frequency of breast cancer attributable to BRCA1 in a population-based series of American women. *JAMA*, 279: 915-21, 1998.

[45] Panguluri, R. C. K., Brody, L. C., Modali, R., Utley, K., Adams-Campbell, L., Day, A. A., Whitfield-Broome, C. *BRCA1* mutations in African Americans. *Hum Genet*, 105: 28-31, 1999.

[46] Press, N. A., Yasui, Y., Reynolds, S., Durfy, S. J., and Burke, W. Women's interest in genetic testing for breast cancer susceptibility may be based on unrealistic expectations. *Am J Med Genet*, 99: 99-110, 2001.

[47] Shen D., Wu, Y., Subbarao, M., Bhat, H., Chillar, R., and Vadgama, J. V. Mutation analysis of BRCA1 gene in African American patients with breast cancer. *J Natl Med Assoc*, 92: 29-35, 2000.

[48] Shih, H. A., Couch, F. J., Nathanson, K. L., Blackwood, M. A., Rebbeck, T. R., Armstrong, K. A., Calzone, K., Stopfer, J., Seal, S., Stratton, M. R., and Weber, B. L. BRCA1

and BRCA2 mutation frequency in women evaluated in a breast cancer risk evaluation clinic. *J Clin Oncol*, 20: 994-99, 2002.

[49] Thompson, H. S., Valdimarsdottir, H. B., Duteau-Buck, C., Guevarra, J., Bovbjerg, D. H., Richmond-Avellaneda, C., Amarel, D., Godfrey, D., Brown, K., and Offit, K. Psychosocial predictors of BRCA counseling and testing decisions among urban African-American women. *Cancer Epidemiol Biomarkers Prev*, 11: 1579-85.

[50] Corbie-Smith, G., Flagg, E. W., Doyle, J. P., and O'Brien, M. A. Influence of usual source of care on differences by race/ethnicity in receipt of preventive services. *J Gen Intern Med*, 17: 458-464, 2002.

[51] Selvin, E. and Brett, K. M. Breast and cervical cancer screening: sociodemographic predictors among white, black, and hispanic women. *Am J Public Health*, 93: 618-623, 2003.

[52] Walls, C. A., Rhodes, K. V., and Kennedy, J. J. The emergency department as usual source of medical care: estimates from the 1998 national health interview survey. *Acad Emerg Med*, 9: 1140-1145, 2002.

[53] Pakilit, A. T., Kahn, B. A., Petersen, L., Abraham, L. S., Greendale, G. A., and Ganz, P. A. Making effective use of tumor registries for cancer survivorship research. *Cancer*, 92: 1305-1314, 2001.

[54] Freimuth, V. S., Quinn, S. C., Thomas, S. B., Cole, G., Zook, E., and Duncan, T. African Americans' views on research and the Tuskegee Syphilis Study. *Soc Sci Med*, 52: 797-808, 2001.

[55] Hughes, C., Gomez-Caminero, A., Benkendorf, J., Kerner, J., Isaacs, C., Barter, J., and Lerman, C. Ethnic differences in knowledge and attitudes about BRCA1 testing in women at increased risk. *Patient Educ Couns*, 32: 51-62, 1997.

[56] Vastag, B. Researchers say changes needed in recruitment policies for NIH-trials. *JAMA*, 289: 536-537, 2003.

[57] Tejeda, H. A., Green, S. B., Trimble, E. L., Ford, L., High, J. L., Ungerleider, R. S., Friedman, M. A., and Brawley, O. W. Representation of African Americans, Hispanics, and Whites in national cancer institute cancer treatment trials. *J Natl Cancer Inst*, 88:812-816, 1996.

Table 1. Hereditary Breast Cancer Studies

Reference ⁽¹⁾ [Geographic Location] (Reference Number)	Study Objective {Type of study} [†]	Study Design	Recruitment Source	Recruitment Strategy
Anton-Culver et al., 2000 [CA] (35)	To evaluate the frequency of BRCA1 mutations in women with breast and ovarian cancer. {E/P}	Cohort	• State cancer registry	<ul style="list-style-type: none"> • <u>Active</u> – Physicians notified about contacting patients identified from registry; introductory letter mailed to patients; patients were also contacted by telephone to review introductory materials
Armstrong et al., 2002 [PA] (36)	To evaluate interest in genetic testing for BRCA1/2 mutations in a primary care population. {P/B}	Cross-sectional	• Hospital clinic	<ul style="list-style-type: none"> • <u>Active</u> – Mailed survey to women randomly selected from billing records
Benkendorf et al., 1997 ⁽¹⁾ [DC] (37)	To describe attitudes about genetic testing for inherited breast cancer risk among African American and Caucasian women with a family history of breast cancer. {P/B}	Cross-sectional	• Hospital clinic	<ul style="list-style-type: none"> • <u>Active</u> – Br Ca cases identified from tumor registry and contacted by telephone to identify unaffected FDRs; invitation letter mailed to unaffected FDRs • <u>Passive</u> – FDRs informed about study by physicians or brochures located in hospital clinics
Donovan et al., 2000 ⁽¹⁾ [AL] (38)	To evaluate differences in knowledge about breast cancer and interest in genetic testing among African American and Caucasian women. {P/B}	Cross-sectional	• Hospital clinic	<ul style="list-style-type: none"> • <u>Active</u> – Subjects approached by project staff while waiting in hospital clinic
Durphy et al., 1999 ⁽¹⁾ [WA] (39)	To evaluate knowledge and interest in genetic testing among demographically diverse women. {P/B}	Cross-sectional	• Community outreach	<ul style="list-style-type: none"> • <u>Passive</u> – Self referral from mass media, radio announcements, newspapers; media approaches to targeted to ethnic-specific outlets
Gao et al., 2000 ⁽¹⁾ [IL, TX] (40)	To evaluate the prevalence of BRCA1 and BRCA2 mutations in African Americans. {E}	Cohort	• High-risk clinic	<ul style="list-style-type: none"> • <u>Passive</u> – Subjects referred by physicians or self because of family history of cancer
Kinney et al., 2002 ⁽¹⁾ [UT/LA] ^a (41)	To evaluate knowledge about genetic testing and identify predictors of testing intentions in African American BRCA1 kindred. {P/B}	Cross-sectional	• Hereditary breast cancer registry	<ul style="list-style-type: none"> • <u>Active</u> – Mailed study invitation to individuals included a hereditary cancer registry
Lipkus et al., 1999 ⁽¹⁾ [NC] (42)	To identify predictors of genetic test intentions in African American women with and without a family history of breast cancer. {P/B}	Case-control	• Hospital clinic	<ul style="list-style-type: none"> • <u>Active</u> – Breast cancer patients identified from tumor registry; contacted by telephone to identify unaffected FDRs; unaffected FDRs invited to participate in the study by telephone • <u>Active</u> – Unaffected women without family

Reference⁽¹⁾ [Geographic Location] (Reference Number)	Study Objective {Type of study}†	Study Design	Recruitment Source	Recruitment Strategy
Narod et al., 2002 [INT] ^b (43)	To evaluate the association between oral contraceptive use and breast cancer risk in BRCA1/2 mutation carriers. {E}	Case-control	• High-risk clinic	history of cancer identified from hospital clinic records; invited to participate in the study by telephone
Newman et al., 1998 ⁽¹⁾ [NC] (44)	To evaluate the prevalence of BRCA1 mutations in population-based women and to characterize differences in prevalence based on race and clinical factors. {E/P}	Case-control	• Cases, state cancer registry • Controls, public records	<ul style="list-style-type: none"> • <u>Passive</u> – Subjects identified from participants enrolled in genetic counseling and testing protocols • <u>Active</u> – Rapid ascertainment of breast cancer cases from state cancer registry. Controls identified from state division of motor vehicles and health care financing records
Panguluri et al., 1999 ⁽¹⁾ [DC] (45)	To evaluate BRCA1 mutations in African Americans. {E}	Case-control	• Hospital clinic	• <u>Passive</u> – Subjects identified from ongoing epidemiological study of breast cancer in African American women
Press et al., 2001 [WA] (46)	To evaluate attitudes and decision-making about genetic testing. {P/B}	Cross-sectional	• Community outreach	• <u>Passive</u> – Advertisements placed in newspapers and newsletters; flyers displayed at community centers, targeted to ethnic-specific events
Shen et al., 2000 ⁽¹⁾ [CA] (47)	To evaluate BRCA1 mutations in African American breast cancer patients. {E}	Cohort	• Hospital clinic	• <u>Active</u> – Consecutive breast cancer patients identified from individuals treated at oncology clinic
Shih et al., 2002 [MI, PA] (48)	To determine the frequency of BRCA1 and BRCA2 mutations in high-risk individuals. {E}	Cohort	• Hospital clinic	• <u>Passive</u> – Self, physician, and family referrals to genetic counseling and testing protocol
Thompson et al., 2002 ⁽¹⁾ [NY] (49)	To identify predictors of participation in BRCA genetic counseling and testing in African American women. {P/B}	Cohort	• Hospital clinic	• <u>Active</u> – Subjects waiting in clinic approached by project staff; nurse practitioners referred potential subjects for study participation

⁽¹⁾Racially or ethnically targeted study; †E=Epidemiological/Population-based; E/C=Epidemiological/Collaborative; P/B=Psychosocial/Behavioral; E=Epidemiological

^aRegistry maintained in Utah; most participants lived in LA; ^bIncludes subjects recruited from high-risk clinics in foreign countries (i.e., Canada, Europe)

Table 2. Sample Characteristics of Hereditary Breast Cancer Studies

Reference	Recruitment Source	Response Rate	Sample Size	Sample Characteristics (Number of Subjects)
Anton-Culver et al., 2000	<ul style="list-style-type: none"> • Cancer registry 	78%**	793	87.6% Caucasian (695) 0.5% African American (4) 6.9% Hispanic (54) 5% Asian (40)
Armstrong et al., 2002	<ul style="list-style-type: none"> • Hospital clinic 	71%	272	66.5% Caucasian (181) 25.3% African American (69) 4.0% Hispanic (11) 1.1% Other (3)
Benkendorf et al., 1997	<ul style="list-style-type: none"> • Hospital clinic • Community outreach 	71%***	238	76% Caucasian (181) 18% African American (43) 6% Other (14)
Donovan et al., 2000	<ul style="list-style-type: none"> • Hospital clinic 	95%**	220	51% Caucasian (112) 49% African American (108)
Durfy et al., 1999	<ul style="list-style-type: none"> • Community outreach 	Not reported	537	88.3% Caucasian (474) 7.2% African American (39) 1.5% Hispanic (8) 1.1% Asian or Pacific Islander (6) 1.8% Other (10)
Gao et al., 2000	<ul style="list-style-type: none"> • High-risk clinic^{§§} 	Not reported	28	100% African American (28)
Kinney et al., 2002	<ul style="list-style-type: none"> • Hereditary breast cancer registry 	79%	95	100% African American (95)
Lipkus et al., 1999	<ul style="list-style-type: none"> • Hospital clinic 	86%, Cases 70%, Controls	Cases = 130 Controls = 136	100% African American (266)
Narod et al., 2002	<ul style="list-style-type: none"> • High-risk clinic 	Not reported	Cases = 1311 Controls = 1311	<u>Cases</u> 29.8% Jewish (391) 61.1% Other Caucasian (801) 1.1% Black (14) 7.4% French Canadian (97) 0.5% Other non-white (6) 0.1% Missing (1) <u>Controls</u> 31.6% Jewish (414) 57.7% Other Caucasian

Table 2. Sample Characteristics of Hereditary Breast Cancer Studies

Reference	Recruitment Source	Response Rate	Sample Size	Sample Characteristics (Number of Subjects)
				2.1% Black (28) 7.6% French Canadian (100) 0.8% Other non-white (10) 0.4% Missing (5)
Newman et al., 1998	<ul style="list-style-type: none"> Cases, state cancer registry Controls, public records 	77%, Cases 68%, Controls	Cases=211*** Controls=188	<u>Cases</u> 57% Caucasian (120) 42% Black (89) 1% Native American (2) <u>Controls</u> 56% Caucasian (105) 42% Black (79) 1% Asian (2) 1% Other (2)
Panguluri et al., 1999	<ul style="list-style-type: none"> Hospital clinic 	Not reported	Cases, N=45 Control, N=92	100% African American (137)
Press et al., 2001	<ul style="list-style-type: none"> Community outreach 	Not reported	246	32.5% Caucasian (80) 20.3% Ashkenazi Jewish (50) 22% African American (54) 25.2% Native American (62) 100% African American (54)
Shen et al., 2000	<ul style="list-style-type: none"> Hospital clinic 	Not reported	54	100% African American (54)
Shih et al., 2002	<ul style="list-style-type: none"> Hospital clinic 	Not reported	159***	95% Caucasian (151) 2% African American (3) 2% Hispanic (3)
Thompson et al., 2002	<ul style="list-style-type: none"> Hospital clinic 	54%	76	100% African American (76)

***No racial or ethnic differences in response rates.

***Response rate for completion of education session that was required for study participation; African Americans less likely to participate in education session.

IN PRESS CANCER EPIDEMIOLOGY, BIOMARKERS, AND PREVENTION

**Predictors of Participation in Psychosocial Telephone Counseling
Following Genetic Testing for BRCA1 and BRCA2 Mutations**

Chanita Hughes Halbert¹, Lari Wenzel², Caryn Lerman¹, Beth N. Peshkin³, Steven Narod⁴,
Alfred Marcus⁵, Camille Corio³, Tiffani Demarco³, Scarlett Bellamy⁶

Running Title: PARTICIPATION IN PSYCHOSOCIAL TELEPHONE COUNSELING

¹Department of Psychiatry and Abramson Cancer Center, University of Pennsylvania, Philadelphia, PA

²Department of Medicine, Epidemiology Division, University of California-Irvine, Irvine, CA

³Department of Oncology, Lombardi Cancer Center, Georgetown University, Washington, DC

⁴The Centre for Research in Women's Health, Women's College Hospital, Toronto, Canada

⁵Center for Behavioral and Community Studies, AMC Cancer Research Center, Denver, CO

⁶Department of Biostatistics and Epidemiology, University of Pennsylvania, Philadelphia, PA

CORRESPONDING AUTHOR: Chanita Hughes Halbert, Ph.D., University of Pennsylvania, 3535 Market Street, Suite 4100, Philadelphia, PA 19104

Telephone Number (215) 746-7144, Fax Number (215) 746-7140, Electronic Mail:

Chanita@mail.med.upenn.edu

ABSTRACT

Although adjunctive educational and psychosocial programs are now being developed for BRCA1 and BRCA2 (BRCA1/2) mutation carriers, limited information is available about whether mutation carriers will want to receive such programs or about the characteristics of individuals who participate. The goals of the present study were to describe rates of completing a psychosocial telephone counseling (PTC) intervention that was offered to female BRCA1/2 mutation carriers and to identify sociodemographic and psychological factors associated with decisions to complete the intervention. Subjects were 66 BRCA1/2 mutation carriers who were randomized to receive a psychosocial telephone counseling intervention following receipt of genetic test results. Sociodemographic and psychological factors were evaluated prior to notification of assignment to the PTC intervention. Completion of the intervention was determined from study records. Overall, 75.8% of subjects completed the PTC intervention. Compared to unaffected subjects, those affected with breast and/or ovarian cancer were 76% less likely to complete the intervention [OR = 0.24, 95% CI = .06, .98, $p = .05$]. In addition, subjects with higher levels of cancer-specific distress [OR = 4.74, 95% CI = 1.02, 22.03, $p = .05$] and those with greater perceptions of social support [OR = 5.81, 95% CI = 1.29, 26.16, $p = .02$] were also most likely to complete the intervention. The results of this study suggest that while most BRCA1/2 mutation carriers are likely to complete an adjunctive psycho-educational program, personal history of cancer, cancer-specific distress, and perceptions of social support are likely to influence participation.

INTRODUCTION

Genetic testing for BRCA1 and BRCA2 (BRCA1/2) mutations is increasingly being integrated into the clinical management of individuals who have a personal or family history of disease that is suggestive of inherited cancer susceptibility. In accordance with guidelines issued by professional organizations, genetic testing should include pre-test education to facilitate informed decisions about whether or not to have testing, post-test counseling to disclose BRCA1/2 test results and provide recommendations for cancer screening and prevention, and post-disclosure follow-up to answer additional questions and provide referrals [1]. The evidence as to whether genetic testing generates adverse psychological reactions is mixed, with some studies reporting no significant effects on generalized distress [2,3] and other studies revealing specific psychological difficulties such as genetic testing specific distress and uncertainty about the clinical and familial implications of BRCA1/2 test results [4,5]. However, mutation carriers may not be equipped to handle these reactions or the responses from family members [6]. Moreover, even though these issues are addressed as part of genetic counseling, there may not be sufficient time to explore these concerns during the test results disclosure session, especially as issues related to the familial impact of testing and decisions about cancer screening and prevention are likely to unfold over time. There have been some recent efforts to develop and evaluate adjunctive educational and psychosocial interventions to address concerns related to medical decision-making and familial issues following genetic testing for BRCA1/2 mutations [6-8]. However, little is known about whether participants in genetic testing will want to receive such interventions, or about the characteristics of individuals who participate versus those who decline. This paper addresses these questions in a sample of BRCA1/2 mutation carriers.

Previous studies suggest that interest in psycho-educational programs following testing may be high among BRCA1/2 mutation carriers. For example, more than 60% of female BRCA1/2 mutation carriers reported that support groups are needed following test results disclosure [9]. Similar results were obtained in a qualitative study of post-test needs among high-risk individuals; about 40% of BRCA1/2 mutation carriers reported that they would be interested in participating in a support group following disclosure of test results [10]. However, high levels of interest in psycho-educational or support programs following testing may not translate into high rates of participation. Only about one-third of BRCA1/2 mutation carriers who said that support groups were needed indicated that they would participate in this type of program [9]. However, data regarding participation in psycho-educational programs following disclosure of positive BRCA1/2 test results are not available.

We conducted a randomized trial to evaluate whether the psychological and behavioral outcomes of BRCA1/2 testing are improved among mutation carriers by providing a psychosocial counseling intervention in addition to standard genetic counseling. An innovative feature of this intervention was that it was delivered by telephone in order to increase the feasibility and acceptability to genetic testing participants. While greater convenience and anonymity may be advantages of telephone counseling [11-13], BRCA1/2 mutation carriers may still decline to participate in post-test psychosocial counseling. Therefore, the present study evaluated rates of completing the psychosocial telephone counseling intervention that was offered following receipt of positive genetic test results. In this report, we only evaluated completion of the telephone counseling intervention because it was offered as an adjunct to standard genetic counseling and required individuals to complete a series of telephone sessions over a five-week period following receipt of their test results. We were also interested in

identifying sociodemographic and baseline psychological factors having independent associations with completing the intervention. Information on the rates and determinants of completing post-test psychosocial counseling will provide important information on the need for and uptake of these types of programs among BRCA1/2 mutation carriers.

MATERIALS AND METHODS

Study Population

Eligible subjects included female BRCA1/2 mutation carriers ages 18 and older who received genetic counseling and testing through research programs at the Georgetown University Medical Center in Washington, DC and the Women's College Hospital in Toronto, Canada. Genetic counseling and testing were provided at no cost through both programs. Persons ineligible to participate in the study included BRCA1/2 mutation carriers who were in palliative care for metastatic breast cancer or recurrent ovarian cancer, males, and individuals who were not able to provide informed consent because of a psychiatric or cognitive disorder.

Procedures

This randomized trial was designed to evaluate the effects of psychosocial telephone counseling on psychological functioning and decisions about cancer screening and surveillance among BRCA1/2 mutation carriers. Following completion of test results disclosure, BRCA1/2 mutation carriers were randomized to receive standard genetic counseling (SGC) or standard genetic counseling plus psychosocial telephone counseling (SGC+PTC). Subjects provide consent to be randomized to the intervention during informed consent for pre-test education and test result disclosure. Of 143 BRCA1/2 mutation carriers who were identified, fifteen were

ineligible for randomization to SGC only or SGC+PTC because they had advanced stage breast or ovarian cancer and 2 refused randomization at the test results disclosure session. Subjects who refused to be randomized to the intervention were excluded from this analysis; thus, of the remaining 126 BRCA1/2 mutation carriers, 66 (52%) were randomized to SGC+PTC and 60 (48%) were randomized to SGC only. Forty-nine families were randomized to SGC and 46 were randomized to SGC+PTC. Subjects randomized to SGC only and SGC+PTC did not differ in terms of sociodemographic characteristics. This report focuses only on participation in SGC+PTC. Detailed information on the study procedures and counseling protocols is provided below.

Following referral, subjects were contacted by telephone to determine eligibility using a structured baseline interview. This interview took approximately forty minutes to complete and included measures of sociodemographic characteristics, personal and family history of cancer, and psychological functioning. Following completion of the baseline telephone interview, eligible subjects were invited to participate in the genetic counseling and testing programs at each center. These programs at both centers included pre-test education and test results disclosure sessions that were conducted by a genetic counselor and lasted about 60 to 90 minutes. To ensure standardization, genetic counselors at both sites used similar protocols to provide pre-test education and to disclose BRCA1/2 test results. Following disclosure of test results, eligible subjects were randomized to receive Standard Genetic Counseling Only (SGC) or Standard Genetic Counseling plus Psychosocial Telephone Counseling (SGC+PTC). Relatives of BRCA1/2 mutation carriers were invited to participate in the study after a risk-conferring BRCA1/2 gene alteration was identified in a family member (e.g., proband) and were randomized to the same intervention group as their relative. One month following disclosure of

BRCA1/2 test results, subjects were contacted for a follow-up telephone interview to re-assess psychological functioning. This interview also served as the baseline assessment for the psychosocial telephone counseling (PTC) intervention. Subjects who were randomized to the SGC+PTC intervention were notified about their study assignment at the end of this interview. Subjects could decline to participate in the intervention when notified of their study assignment at the end of this interview and could also decline to participate in the intervention during the initial orientation call completed by the PTC counselor.

Counseling Protocols

Standard Genetic Counseling (SGC) Only. The SGC only protocol consisted of pre-test education, test results disclosure, and post-disclosure follow-up. During pre-test education, subjects received information about hereditary breast and ovarian cancer, gene identification and mutation testing, and the benefits, limitations, and risk of genetic testing. During the test results disclosure session, BRCA1/2 test results were disclosed along with information about the risk for developing cancer and individualized guidelines for surveillance and prevention. Supportive counseling that included an assessment of emotional responses, identification of at-risk relatives, and discussion of family communication issues, was also provided as part of this session. All subjects also received a written summary letter that included an interpretation of their BRCA1/2 test result and medical management guidelines. The test results disclosure session was audio taped after obtaining written informed consent. Approximately two weeks after the disclosure session, subjects were contacted by their genetic counselor to complete a post-disclosure follow-up. The post-disclosure follow-up was completed by telephone and was designed to informally

assess how subjects were coping and assimilating their test results, answer any questions about their results, and provide additional referrals, if needed.

Standard Genetic Counseling plus Psychosocial Telephone Counseling (SGC+PTC). The SGC+PTC protocol consisted of the pre-test education session, test results disclosure session, and post-disclosure follow-up described above. Following the 1-month follow-up telephone interview, subjects assigned to SGC+PTC also received a psychosocial telephone counseling intervention. The PTC intervention was developed based on the Transactional Model of Stress and Coping and consisted of five semi-structured telephone counseling sessions that were delivered over a 5-week period by Master's level counselors affiliated with the Cancer Information Line of the AMC Cancer Research Center [12]. Written materials, designed to accompany each thematic issue (e.g., family communication, medical decision-making, and emotional reactions) addressed during the intervention, were also mailed to subjects after completion of the 1-month follow-up telephone interview. These materials were mailed to subjects before they were contacted by the PTC counselor for the intervention. To facilitate the transfer from standard genetic counseling to the PTC intervention, a transition protocol was used. This transition was completed by telephone and consisted of a case review between the genetic counselor and the PTC counselor. Prior to the transition call, the PTC counselor listened to the audiotape of the disclosure session and reviewed the written test results summary letter. During the transition call, the genetic counselor and PTC counselor discussed the subject's primary issues surrounding medical decision-making, family concerns, and emotional reactions. After the transition call was completed, the PTC counselor contacted subjects for an initial orientation call. During this call, the purpose of the intervention was reviewed and the telephone counseling

sessions were scheduled. Following completion of the orientation call, subjects were contacted for the first telephone counseling session.

The first telephone counseling session of the PTC intervention (session 1) consisted of a semi-structured clinical assessment interview that was designed to allow the subject to describe her experiences with and reactions to her BRCA1/2 test results. Sessions 2 through 4 were individualized to the concerns raised by subjects within the domains of making medical decisions, managing family concerns, and emotional reactions following receipt of a positive BRCA1/2 test result. The order in which the sessions were delivered was determined based on the priority area identified by subjects during session 1. The last session of the intervention (session 5) focused on integration and closure of each issue that had been addressed during the intervention. An implementation plan was also developed during session 5 to execute the short- and long-term goals that were established during the intervention. Each telephone counseling session lasted about 60 to 90 minutes and was audio taped after obtaining informed consent.

Measures

Predictor Variables. We selected factors that prior studies [5,6,14] have shown to be areas in which BRCA1/2 mutation carriers are likely to experience difficulty following test results disclosure to evaluate as predictors of completing the intervention.

Sociodemographics. Age, marital status, income level, education, and employment status were obtained during the baseline telephone interview.

General and Cancer Specific Distress. We used the Impact of Events scale (IES) [15] to evaluate the frequency of intrusive thoughts about cancer and attempts to avoid these thoughts and feelings. The IES has been validated among women from hereditary breast cancer families

[16] and has been used to evaluate the impact of genetic testing among high-risk individuals [17]. The IES had excellent internal consistency in this sample (Cronbach's $\alpha = .90$). We used the total score for the IES in this study; possible scores ranged from 0 to 72. We also measured general distress using the Hopkins Symptom Checklist-25 (HSCL-25) [18,19]. The HSCL-25 is a 25-item Likert-style scale that evaluates the presence and severity of anxiety and depression symptoms during the previous month. The HSCL-25 has been used in prior studies to evaluate psychological functioning among women at high risk for having a BRCA1/2 gene alteration [20] and had excellent internal consistency in this sample (Cronbach's $\alpha = .90$). Possible scores for the HSCL-25 ranged from 25-100.

Social Support. We measured social support using the appraisal sub-scale of the Interpersonal Support Evaluation List (ISEL) [21]. The ISEL is a well-validated self-report measure of perceptions of social support. The appraisal sub-scale includes 10 Likert-style items that evaluate perceptions of the availability of individuals with whom important issues can be discussed. The appraisal scale had excellent internal consistency in this sample (Cronbach's $\alpha = .89$) and possible scores ranged from 0 to 23. We also evaluated receipt of social support using a binary item that asked respondents to indicate if they had seen a counselor for emotional support.

Cognitive Appraisals about Genetic Testing. We evaluated cognitive appraisals about BRCA1/2 test results in terms of perceptions of stress and confidence using two new questionnaires that were developed based on the Transactional Model of Stress and Coping [14, 22-24]. To evaluate perceptions of stress, we used five Likert-style items to evaluate perceptions of stress regarding the risk of developing cancer, decisions about risk reduction strategies (i.e., prophylactic surgery) and screening (i.e., mammography), communicating with family members,

and dealing with the familial impact of BRCA1/2 test results (1 = not at all stressful, 2 = a little stressful, 3 = moderately stressful and 4 = very stressful). To evaluate perceptions of confidence, we used five Likert-style items to assess perceptions of one's confidence in their ability to manage the familial implications of genetic testing, communication of results to family members, and decision-making about cancer prevention and surveillance (1 = not at all confident, 2 = somewhat confident, 3 = moderately confident, 4 = very confident). For both scales, scores ranged from 5 to 20, with higher scores indicating greater perceptions of stress and confidence. Both instruments had good internal consistency in this sample (Cronbach's alpha for primary appraisal = .75 and Cronbach's alpha for secondary appraisal = .73).

Outcome Variable

Completion of the SGC+PTC Intervention. Completion of the SGC+PTC intervention was determined from study records. Subjects who accepted the invitation and completed all five of the telephone counseling sessions were categorized as participants. Those who declined to participate in the intervention, could not be reached for any of the sessions, or withdrew from the intervention after completing at least one session were categorized as non-participants.

RESULTS

Participation in Psychosocial Telephone Counseling. As shown in Table 1, the majority of subjects who were randomized to SGC+PTC were under age 50 (76%), married (74%), employed (74%), and were college graduates (77%). Ninety-seven percent of subjects were Caucasian. Of the 66 BRCA1/2 mutation carriers who were randomized to SGC+PTC, 50 (75.8%) completed the intervention and 16 (24.2%) did not complete the intervention. Of those who did not complete the intervention, most (n=13) declined to participate in the intervention

and did not complete any sessions. Those who withdrew (n=2) from the intervention completed 1 to 3 sessions. One subject could not be reached for any of the telephone counseling sessions. Subjects who declined to complete the 1-month follow-up interview (n=1) and those who had incomplete data for one or more predictor variables (n=3) were excluded from subsequent analyses; thus, the data presented below compare the 47 subjects who completed the PTC intervention to the 15 subjects who did not complete the intervention (91% of subjects who were randomized to the intervention).

Predictors of Completing the Intervention. As shown in Table 1, cancer history, education level, and employment status were associated significantly with completing the PTC intervention. Subjects who did not report a personal history of cancer, those who were college graduates, and were employed were most likely to complete the intervention. Table 2 shows the association between psychological factors and completion of the intervention. Of these factors, greater levels of cancer specific distress, greater perceptions of appraisal support, and lower perceptions of confidence were associated significantly with completing the PTC intervention.

To identify independent predictors of completing the PTC intervention, we conducted backward stepwise logistic regression. Because multiple family members were included in the analysis, we used a Generalized Estimating Equation (GEE) approach to generate the regression model while controlling for potential intra-familial correlations. In addition, continuous psychological variables were re-coded into binary variables using the median split to facilitate the interpretation of results. On Step 1, perceived confidence was removed from the model (Likelihood Ratio Test = 0.27, $p = .60$). Employment status was removed on Step 2 (Likelihood Ratio Test = 1.17, $p = .28$). None of the remaining variables could be removed from the model;

thus, the final model included education level, cancer history, cancer-specific distress, and perceptions of social support. As shown in Table 3, subjects affected with cancer were 76% less likely to complete the intervention compared to subjects without a personal history of cancer (Odds Ratio = 0.24, 95% Confidence Interval = .06, .98, $p = .05$) whereas subjects with greater levels of cancer specific distress were about four times more likely to complete the intervention compared to subjects with lower levels of distress (Odds Ratio = 4.74, 95% Confidence Interval = 1.02, 22.03, $p = .05$). Subjects with greater perceptions of appraisal support were also about six times more likely to complete the intervention compared to subjects with lower perceptions of support (Odds Ratio = 5.81, 95% Confidence Interval = 1.28, 26.16, $p = .02$).

DISCUSSION

Although participation in genetic counseling and testing has been evaluated in prior reports [2,25-27], this is the first study to evaluate completion of a psychosocial telephone counseling intervention offered to BRCA1/2 mutation carriers following receipt of genetic test results. In previous studies, about 40% to 60% of BRCA1/2 mutation carriers indicated that support groups were needed for mutation carriers [9,10]; however, only 27% to 34% of respondents said they would be interested in participating in a support group [11,28]. We found that 75.8% of BRCA1/2 mutation carriers who were randomized to receive adjunctive psychosocial telephone counseling completed the intervention. It is possible that delivery of the intervention by telephone is more acceptable to BRCA1/2 mutation carriers than traditional support groups because telephone counseling allows for greater anonymity and convenience. Further, compared to support groups, telephone counseling may provide greater attention to individual concerns related to genetic test results. While it is possible that providing the PTC

intervention within a short time frame following test results disclosure contributed to the completion rates observed in this study, subjects could refuse to be randomized to the intervention and could also decline participation when notified of their assignment to psychosocial telephone counseling. Despite this, the majority of subjects completed all five of the telephone counseling sessions. This finding suggests that levels of interest in post-test support may translate into similar rates of participation in adjunctive counseling programs among female BRCA1/2 mutation carriers. However, the PTC intervention was designed to enhance standard genetic counseling using a format and length that would be convenient and engaging for mutation carriers; therefore, future studies are needed to evaluate participation in post-test counseling programs that are delivered in different formats (e.g., in person) and for longer periods of time.

Previous research has shown that most women would prefer to receive supportive counseling as part of receiving genetic test results for inherited cancer risk [29] and subjects in this study received comprehensive genetic counseling that included pre-test education, post-test counseling, and post-disclosure follow-up. However, the limited time frame during which the test result disclosure was completed may not have been sufficient to address reactions to receiving positive BRCA1/2 test results. Each genetic counseling session lasted about 60 to 90 minutes and during the test results disclosure session, family members at risk for having a BRCA1/2 gene alteration were identified and information about cancer screening and prevention was also discussed. It may not be logistically possible to address all issues related to receiving a positive BRCA1/2 test result during the limited time frame for the test results disclosure session. Offering post-test counseling by telephone following test results disclosure may be one strategy for expanding these services in a way that is acceptable to BRCA1/2 mutation carriers.

However, not all mutation carriers may need more intensive follow-up after receiving genetic test results.

We found that subjects who did not have a personal history of cancer were significantly more likely to complete the PTC intervention compared to those who were affected with breast and/or ovarian cancer. Although our prior study did not detect differences in genetic testing distress or uncertainty between affected and unaffected women [4], it is possible women with a personal history of cancer have fewer decisions to make regarding cancer prevention and screening because of prior cancer treatment. Our prior work has also shown that affected probands communicate their results to some family members within a short time frame following the test results disclosure session [30]. Thus, women affected with cancer may have fewer medical decisions and psychological issues following receipt of their BRCA1/2 test results; this may explain lower rates of completing the PTC intervention among this group. We also found that subjects with greater levels of cancer-specific distress were more likely to complete the intervention compared to subjects with lower levels of distress. Thus, even though prior studies have found that distress levels in high-risk women may not be at the level at which clinical intervention is needed [20], resources that provide short-term follow-up to address specific responses to BRCA1/2 test results may be beneficial to mutation carriers. However, the results of the present study suggest that BRCA1/2 mutation carriers without a personal history of breast or ovarian cancer and those with greater levels of cancer-specific distress may be the most receptive to these services.

It is interesting to note that subjects who had greater levels of appraisal support were about six times more likely to complete the PTC intervention compared to subjects with lower levels of support. One possible explanation for this finding is that the resources that mutation

carriers, especially those unaffected, are likely to seek for support for concerns related to their BRCA1/2 test result may not be able to address these needs sufficiently. Our prior work has shown that BRCA1/2 mutation carriers communicated their genetic test results to significantly more sisters than noncarriers expressly to obtain emotional support as well as advice about cancer screening and prevention [30]. It is possible that once emotional support is engaged through family discussions the participant is primed to further engage in a supportive intervention with greater comfort, ease, and sense of social acceptability. This might stand in contrast to those less likely to complete the intervention who perceive lower levels of appraisal support. Psychosocial telephone counseling may provide an additional source of support that is acceptable to BRCA1/2 mutation carriers; however, additional research is needed to evaluate the effects of the PTC intervention on psychological functioning and medical decision-making.

In considering the results of this study, several limitations should be noted. First, the results of this study are based on a small sample of BRCA1/2 mutation carriers who were enrolled in a genetic counseling and testing research study in which these services were provided at no cost. We had approximately 70% power to detect moderate differences in completing the intervention between affected and unaffected subjects and among subjects who were above and below median levels of psychological factors; thus, additional studies are needed to evaluate completion of post-test counseling among larger samples of BRCA1/2 mutation carriers. Further, our analysis was limited to completion of a psychosocial telephone counseling that was offered as part of a research program. However, subjects could decline randomization to the intervention and could also decline participation in the telephone counseling sessions. An additional limitation may be that most subjects (81%) self-referred to genetic counseling and testing. However, referral mechanism was not associated significantly with completing the

intervention. Thus, rates of completing the post-test counseling intervention are not likely to have been biased by study procedures.

Despite these limitations, this is the first study to evaluate completion of follow-up counseling among BRCA1/2 mutation carriers. The results of the present study suggest that most BRCA1/2 mutation carriers will elect to participate in short-term follow-up counseling, but personal experiences with cancer diagnosis, cancer distress, and perceptions of social support are likely to influence completion of these types of interventions. The results of the study also have implications for provision of genetic counseling services. Most subjects completed the intervention, which suggests that individuals are receptive to telephone counseling. While current recommendations for genetic testing for inherited cancer risk include provision of in-person genetic counseling [1], genetic counseling by telephone may also be well received among individuals considering testing.

ACKNOWLEDGEMENTS

This research was supported by the National Human Genome Research Institute grant #HG01846. Preparation of this manuscript was supported by Department of Defense grant #DAMD17-00-1-0262 (to CHH). We would like to acknowledge Barbara Brogan, M.S. RN, Elizabeth Hoodfar, M.S., CGC and Danielle Hanna, CGC for providing genetic counseling to study participants, V. Holland LaSalle for conducting telephone interviews, and Wilma Higginbotham for assistance with manuscript preparation. Last, but not least, we would like to thank study participants for their contribution to this research.

REFERENCES

- [1] American Society of Clinical Oncology. Policy update on genetic testing for cancer susceptibility. *J. Clin. Oncol.*, 21: 2397-2406, 2003.
- [2] Lerman C., Narod S., Schulman K., Hughes C., Gomez-Caminero A., Bonney G., Gold K., Trock B., Main D., Lynch J., Fulmore C., Synder C., Lemon S. J., Conway T., Tonin P., Lenoir G., and Lynch H. BRCA1 testing in families with hereditary breast-ovarian cancer. A prospective study of patient decision making and outcomes. *JAMA*, 275: 1885-1892, 1996.
- [3] Croyle R. T., Smith K. R., Botkin J. R., Baty B., and Nash J. Psychological responses to BRCA1 mutation testing: preliminary findings. *Health Psychol.*, 16: 63-72, 1997.
- [4] Cella D., Hughes C., Peterman A., Chang C. H., Peshkin B. N., Schwartz M. D., Wenzel L., Lemke A., Marcus A. C., and Lerman C. A brief assessment of concerns associated with genetic testing for cancer: the multidimensional impact of cancer risk assessment (MICRA) questionnaire. *Health Psychol.*, 21: 564-572, 2002.
- [5] Dorval M., Patenaude A. F., Schneider K. A., Kieffer S. A., DiGianni L., Kalkbrenner K. J., Bromberg J. I., Basili L. A., Calzone K., Stopfer J., Weber B. L., and Garber J. E. Anticipated versus actual emotional reactions to disclosure of results of genetic tests for cancer susceptibility: findings from p53 and BRCA1 testing programs. *J. Clin. Oncol.*, 18: 2135-2142, 2000.

- [6] Speice J., McDaniel S. H., Rowley P. T., and Loader S. Family issues in a psychoeducation group for women with a BRCA mutation. *Clin. Genet.*, 62: 121-127, 2002.
- [7] Kaufman E. M., Peshkin B. N., Lawrence W. F., Shelby R., Isaacs C., Brown K., Rispoli J., O'Neill S., Hurley K., DeMarco T., Brogan B., Grumet S., Jandorf L., McKenna K., Valdimarsdottir H., and Schwartz M. D. Development of an interactive decision aid for female BRCA1/BRCA2 carriers. *J. Genet. Couns.*, 12: 109-129, 2003.
- [8] Tiller K., Meiser B., Reeson E., Tucker M., Andrews L., Gaff C., Kirk J., Phillips K. A., and Friedlander M. A decision aid for women at increased risk for ovarian cancer. *Int. J. Gynecol. Cancer*, 13: 15-22, 2003.
- [9] Metcalfe K. A., Liede A., Hoodfar E., Scott A., Foulkes W. D., and Narod S. A. An evaluation of needs of female BRCA1 and BRCA2 carriers undergoing genetic counseling. *J. Med. Genet.*, 37: 866-874, 2000.
- [10] Di Prospero L. S., Seminsky M., Honeyford J., Doan B., Franssen E., Meschino W., Chart P., and Warner E. Psychosocial issues following a positive result of genetic testing for BRCA1 and BRCA2 mutations: findings from a focus group and a needs-assessment survey. *CMAJ*, 164: 1005-1009, 2001.
- [11] Gotay C. C., and Bottomley A. Providing psycho-social support by telephone: what is its potential in cancer patients? *Eur. J. Cancer Care*, 7: 225-231, 1998.

[12] Marcus A. C., Garrett K. M., Kulchak-Rahm A., Barnes D., Dortch W., and Juno S. Telephone counseling in psychosocial oncology: a report from the cancer information and counseling line. *Patient Educ. Couns.*, 46: 267-275, 2002.

[13] McBride C. M., and Rimer B. K. Using the telephone to improve health behavior and health service delivery. *Patient Educ. Couns.*, 37: 3-18, 1999.

[14] Halbert C. H., Schwartz M. D., Wenzel L., Lerman C. Cognitive appraisals following genetic testing for BRCA1 and BRCA2 mutations. *J. Behav. Med.* In Press.

[15] Horowitz M., Wilner N., and Alvarez W. Impact of event scale: a measure of subjective stress. *Psychosomatic Medicine*, 41: 209-218, 1979.

[16] Thewes B., Meiser B., and Hickie I. B. Psychometric properties of the impact of event scale amongst women at increased risk for hereditary breast cancer. *Psychooncology*, 10: 459-468, 2001.

[17] Lerman C., Hughes C., Lemon S. J., Main D., Snyder C., Durham C., Narod S., and Lynch H. T. What you don't know can hurt you: adverse psychologic effects in members of BRCA1-linked and BRCA2-linked families who decline genetic testing. *J. Clin. Oncol.*, 16: 1650-1654, 1998.

- [18] Derogatis L. R., Lipman R. S., Rickels K., Uhlenbuth E. H., and Covi L. The hopkins symptom checklist (HSCL): a self-report symptom inventory. *Behav. Sci.*, 19: 1-15, 1974.
- [19] Hesbacher P. T., Rickels K., Morris R. J., Newman H., and Rosenfeld H. Psychiatric illness in family practice. *J. Clin. Psychiatry*, 41: 6-10, 1980.
- [20] Coyne J. C., Benazon N. R., Gaba C. G., Calzone K., and Weber B. L. Distress and psychiatric morbidity among women from high-risk breast and ovarian cancer families. *J. Consult. Clin. Psychol.*, 68: 864-874, 2000.
- [21] Cohen, S., Mermelstein, R., and Karmack, T. Measuring the functional components of social support. *In*: I. Sarason and B. Sarason, (eds.) *Social Support: Theory, Research, and Applications*, pp. 73-94. Martinus Nijhoff, Dordrecht, Netherlands. (1985).
- [22] Chang E. C. Dispositional optimism and primary and secondary appraisal of a stressor: controlling for confounding influences and relations to coping and psychological and physical adjustment. *J. Pers. Soc. Psychol.*, 74: 1109-1120, 1998.
- [23] Lazarus R. S., and Folkman S. *Stress, Appraisal, and Coping*. New York: Springer, 1984.
- [24] Lerman C., and Glanz K. Stress, coping, and health behavior. *In*: K. Glanz, F. M. Lewis, and B. Rimer, (eds). *Health Behavior and Health Education: Theory, Research, and Practice* pp.113-138. California: Jossey-Bass Publishers, 1997.

- [25] Schwartz M. D, Hughes C., Roth J., Main D., Peshkin B. N., Isaacs C., Kavanagh C., and Lerman C. Spiritual faith and genetic testing decisions among high-risk breast cancer probands. *Cancer Epidemiol., Biomark., Prev.*, 9: 381-385, 2000.
- [26] Biesecker B. B., Ishibe N., Hadley D. W., Giambresini T. R., Kase R. G., Lerman C., and Struwing J. P. Psychosocial factors predicting BRCA1/BRCA2 testing decisions in members of hereditary breast and ovarian cancer families. *Am. J. Med. Genet.*, 93: 257-263, 2000.
- [27] Armstrong K., Calzone K., Stopfer J., Fitzgerald G., Coyne J., and Weber B. Factors associated with decisions about clinical BRCA1/2 testing. *Cancer Epidemiol., Biomark., Prev.*, 9: 1251-1254, 2000.
- [28] Dorval M., Maunsell E., Dugas M. J., and Simard J. Support groups for people carrying a BRCA mutation. *JAMC*, 165: 740, 2001.
- [29] Audrain J., Rimer B., Cella D., Garber J., Peshkin B. N., Ellis J., Schildkraut J., Stefanek M., Vogel V., and Lerman C. Genetic counseling and testing for breast-ovarian cancer susceptibility: what do women want? *J. Clin. Oncol*, 16: 133-138, 1998.
- [30] Hughes C., Lerman C., Schwartz M., Peshkin B. N., Wenzel L., Narod S., Corio C., Tercyak K. P., Hanna D., Isaacs C., and Main D. All in the family: an evaluation of the process and content of sister's communication about BRCA1 and BRCA2 genetic test results. *Am. J. Med. Genet.*, 107: 143-150, 2002.

Table 1. Sample Characteristics and Bivariate Association between Completion of Psychosocial Telephone Counseling and Sociodemographic Factors and Counseling Utilization (n = 62)

Variable	Level	n (%)	%Participate	χ^2
Age	≤ 50	47 (76%)	79%	0.90
	> 50	15 (24%)	67%	
Marital Status	Married	46 (74%)	72%	1.61
	Not married	16 (26%)	88%	
Education Level	College graduate or higher	49 (79%)	82%	4.32*
	Some college or less	13 (21%)	54%	
Employment Status	Employed	46 (74%)	83%	4.50*
	Not employed	16 (26%)	56%	
Income Level	> \$75,000	33 (55%)‡	82%	1.08
	< \$75,000	27 (45%)	70%	
Cancer History	Affected	33 (53%)	64%	5.69*
	Unaffected	29 (47%)	90%	
Obtained Counseling	Yes	11 (18%)	73%	0.07
	No	51 (82%)	76%	

‡Two subjects were missing data for income.

*p < .05

Table 2. Psychological Factors Associated with Completing the PTC Intervention (n=62)

Variable	Participants Mean (S.D.)	Non-Participants Mean (S.D.)
General Distress	35.5 (8.8)	33.9 (10.0)
Cancer Specific Distress**	22.60 (20.1)	10.31 (11.6)
Appraisal Support**	5.66 (5.3)	2.51 (2.8)
Primary Appraisal	10.72 (3.3)	11.21 (3.7)
Secondary Appraisal*	16.82 (2.7)	18.33 (1.8)

**p < .01, *p < .05

Table 3. Multivariate Model Predicting Completion of Psychosocial Telephone Counseling (n=62)

Variable	Levels	OR [†]	95% CI ^{††}	P-value
Cancer History	Affected Unaffected (Referent)	0.24 1.00	0.06, 0.98	.05
Education Level	College graduate or higher Some college or less (Referent)	4.28 1.00	0.94, 19.50	.06
Cancer Specific Distress	Above median ^{†††} Below median (Referent)	4.74 1.00	1.02, 22.03	.05
Appraisal Support	Above median ^{††††} Below median (Referent)	5.81 1.00	1.29, 26.16	.02

[†]OR=Odds Ratio; ^{††}CI=Confidence Interval; ^{†††}Median Value =16; ^{††††}Median Value = 4